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THE PHILOSOPHY OF TUMOUR-DISEASE.



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THE PHILOSOPHY OF TUMOUR-DISEASE :

A RESEARCH FOR PRINCIPLES OF ITS TREATMENT.

BY

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AND EVOLUTION AND THE SCIENCE OF MEDICINE," ETC.



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PREFACE.

THE beginning of the present research is incorporated in a volume entitled "Dissolution and Evolution and the Science of Medicine" (Longmans & Co.). While attempting in that work to give coherence to the essentials of Pathology I have set forth a new conception of tumour-disease. It is now intended to bring this conception into closer embrace with the truth by putting it through the crucible of a more extended and searching examination of the subject.

Of the problems in medicine, at present pressing for solution, that concerned with the nature, origin, and causes of tumours is certainly the weightiest. Momentous interest attaches to it from the possible discovery of some preventive or cure for cancer. Then the problem is of great intrinsic difficulty. Of this anyone may convince himself by the reflection that tumour-disease has existed from the earliest historical periods; that it has been among the most observed of all diseases; and that upon the question of its nature and causation there are as yet no signs of unanimity.

So divergent are men's views upon the subject that to many it may seem a hopeless task to search for a basis of reconciliation without some years of further observation and experiment.

I am not of this opinion, but believe that in the identification of neoplasia with the phenomenon of histogenic dissolution (§ 4) there has been discovered the means by which infinite rays of scattered truth may be gathered into one large illuminating conception. The need is less for new data than for a principle that will fuse into a whole the masses of facts already garnered but that lie obscured by disregard.

Is it then claimed for the hypothesis developed in these pages that it supplies a truthful explanation of tumour-disease? Of this the work itself must be witness, but the importance of the subject demands a word or two here touching one practical issue of the investigation. Do the results afford any hope that cancer is a preventable disease? The answer is distinctly in the affirmative. If the conclusions arrived at are true, cancer is not, as nearly all believe, an inevitable malady for many men and women, but is dependent on causes for the most part avoidable. Against cancer of the tongue, lips, and some other parts, there is almost certainly available at the present moment a perfect prophylaxis, and a partial prophylaxis against the same disease in the stomach, uterus, breast, and elsewhere. (See chapter xi.)

It may be well to say something as to the credentials of what is new and distinctive of the present hypothesis of tumour-disease. The affiliation of neoplasia with a mode of reproduction among the Protozoa was the result of a prolonged examination of all the classes of facts established in connection

with the subject ; and while the hypothesis, when first conceived, transcended the facts in identifying neoplasia with histogenic dissolution, it yet remained rooted in the solid ground of reality. Histogenic dissolution is not a mere formal assumption, or thing of the imagination, but is as real as tumour-disease. There is no constituent of the theory that does not ultimately rest on observable phenomena.

Where possible, with few exceptions, I have presented the inductive evidence in the words of the original reports. Besides the saving of time and trouble it greatly furthers the object of a work with the character of the present one to retail facts as they are described by those who have observed them. If paraphrased, the language of an observer chances to lose both in force and precision, and the reproduction unaltered of the statements of several observers of the same fact tends, by neutralizing "personal equations," to minimize the natural defects of language as the exponent of truth. But the gain to truth is a loss to literary composition in its artistic aspects.

It is due to the authors of the many illustrative cases adduced, to say that, in nearly every instance, the reports are abridged to meet the particular purposes of the inquiry. A certain prolixity and repetition in the cases and commentations has seemed to be necessitated by the perplexing guises of the phenomena investigated.

The literature of tumour-disease is of vast volume and my incursions into it have involved not a little labour ; but this

has been materially lightened by the help and kindness of Mr. James B. Bailey, the librarian of the Royal College of Surgeons. It is pleasant to have this opportunity of expressing my thanks and sense of the advantage I have thus enjoyed in common with every other worker in the library of the College.

LONDON, *June*, 1890.

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ERRATA.

Page 28, six lines from top, *for* issue *read* tissue.

„ 138, four lines from top, *for* breast *read* bust, and
for mamma *read* mammæ.

THE PHILOSOPHY OF TUMOUR-DISEASE.

INTRODUCTORY.

As stated in the preface, the present essay is intended to develop and verify a conception resulting from a previous investigation of the nature and origin of tumours. Our task therefore will largely consist in the examination of groups of evidential facts; and in order that the bearing of these facts may be appreciated as they successively appear, it will be needful at the outset to equip the reader with the hypothesis we have espoused. Hence the first chapter will be devoted to presenting such an outline of the hypothesis as will serve the purpose of a scheme for building the organized structure of a consistent theory. Of course, as an exceedingly generalized statement, this outline merely adumbrates the truth about tumour-disease. A practically useful conception can only be obtained by saturating oneself with relevant facts of every order. It is expected of the entire work to unfold a more or less finished explanation of the phenomena it is desired to understand.

Having put forward the view here held as to the nature and origin of tumours we shall next consider to what extent the

facts support, enlarge, or conflict with, this view, and how far they are interpretable by it. One or two detached problems will then be studied, and it will remain, finally, to extract from the research some lessons upon the prevention and treatment of tumours.

CHAPTER I.

OUTLINE OF A HYPOTHESIS OF THE ORIGIN AND NATURE OF
TUMOURS.

The source of the Cellular elements of Tumours.—The Self-dependence of Tumours.—Explanation of the Self-dependence of Tumours: Neoplasia identified with Genesis in the Protozoa.—The Conditions of the Genesis of Tumours: Histogenic Dissolution.—The Resistance of the Organism to the Growth of Tumours.—Recapitulation and Conclusion.

§ 1. *The Source of the Cellular elements of Tumours.*

It is very important to bear constantly in mind one or two points as to the kind of growths with which we are here concerned. The tumours whose phenomena we are to investigate are the simple- and compound-tissue tumours; those tumours known as cancers, sarcomas, adenomas, fibromas, chondromas, or other neoplasms classed for their representation of the tissues of the body. What are known as infective tumours or granulomata—such as the growths of syphilis, tubercle, lupus, or leprosy—are not included; nor are the cystomata and teratomata. Shortly there will be occasion to consider in detail the relations to one another of the simple- and compound-tissue tumours, but it will be well to note now that throughout them there is conceived an essential unity. The difference, for example, between the malignant cancers or sarcomas and the benign growths, is not one of specific nature and causation, but simply one of development and structure. A sarcoma is an immature fibroma, or other growth of the connective tissue class, and a cancer of glands is an immature adenoma. Therefore when speaking of tumours collectively the term will be understood to embrace the whole series of simple- and compound-tissue neoplasms.

Secondary tumours being the products of particles detached from primary tumours the facts of their phenomena will not enter into the following hypothesis which is concerned with the nature and *genesis* of tumours, not with their modes of propagation.

It is hardly required to premise that tumours, like other living products of organic being, are cellular in structure. One of the problems first importuning the inquirer for an answer is that of the origin of tumour-cells. It has long been established—the problem has so far been settled—that the cells of tumours are derived in some way from the cells of the corporate organism. By one set of observers the supposition has been formed that the blood in a special, but unexplained, manner and not by its mere nutritive quality, is implicated in the local aggregation of the elements of tumours. “There has been thought by some to be a state of mixture of the blood, such that the substance of the tumour comes out as a *residue*, when other organs have taken their respective shares of nourishment. By others that there is an organizing power in the *blood*, so that it actually pours out material that forms a tumour.”* By still other observers it is conceived that the starting point of a tumour is the superfluous production of cells in the growing embryo (Cohnheim). Cells in excess of those required for normal growth and development are left lying over at various places in the body, and these redundant units under conditions not yet elucidated, eventually multiply and become manifest as tumours. This latter mode of origin has been much advocated, and is known as the origin by embryonic remains. It will, I think, be subsequently seen that these and some other kindred assumptions are serviceable mainly in deepening our sense of need for a more fruitful hypothesis. Referring to Cohnheim’s view, Dr. Fagge says:† “But it is obvious, though Cohnheim does not seem to think so, that such theories afford no explanation whatever of the

* Wilks and Moxon: Pathological Anatomy, 3rd ed., 1889.

† Principles and Practice of Medicine. Edited by Dr. Pye Smith, 2nd ed.

mystery of tumour development. How a fragment of tissue, after lying dormant for years, can produce a carcinoma or a sarcoma still remains entirely unexplained." And, touching the same matter, it is observed by Dr. Payne* that, "It is not enough that a hypothesis should be capable of explaining a series of facts. Before it is accepted as the true explanation, the cause supposed must in the first place be proved to exist, and it must be shown that no other cause would produce the same effects. It is not claimed that the causes assumed by Cohnheim's theory have been proved to exist generally, and therefore, for the present, this theory cannot be accepted as a part of science. But no other explanation has been suggested which accounts for as many facts."

If we discard these attempts to explain the origin of tumours is there an explanation forthcoming with higher claims upon our confidence? The one to which I think we may pledge ourselves with safety accounts for the elements of a tumour by regarding them as out-growths of normal tissue-cells. The process involved in this out-growth is that of asexual multiplication. Cells of epithelium, connective tissue, bone, or muscle, by divisions of their protoplasm, increase in number. Thereupon the new generation begins to grow by further cell-divisions, and it is by such divisions that a visible tumour is ultimately produced.

It will be seen that, according to this view, the process by which a tumour originates and grows is fundamentally the same as the process of normal growth, repair by scar tissue, hypertrophy, and so-called growth by inflammation. It is the same in that increase is effected by the cleavage of tissue-cells. We know, however, that tumour-growth has express and peculiar attributes which distinguish it from normal growth, hypertrophy, and repair, and to perceive one of these distinguishing characters must be our next endeavour.

* A Manual of General Pathology.

§ 2. *The Self-dependence of Tumours.*

A peculiarity of tumour-formation is the inbred capacity of tumours for growing and developing out of relation to the ends of the organism. In natural healthy growth, including repair, we see that the various components of the body are severally limited in their unfolding by a reciprocity of functional and structural adjustment. The size to which a limb will grow is determined by the correlations of the limb with other parts of the body; a heart hypertrophied from any cause has enlarged in proportion as it has been called upon to perform enlarged functions; and the substance of repair in a wound is arrested in its increase when it has filled up the vacancy caused by a previous injury. But such subordination is not characteristic of tumours; both in structure and function a tumour is a segregated mass of units living and propagating independently of the organism except in so far that the latter is its source of nutriment. Tumours have no functional value in the economy; their own simple functions of nutrition, reproduction, and secretion, are carried on quite irrespective of organismal needs. The only union between tumours and the body is that effected by the lymph- and blood-vascular systems; they are not included in the great integrating system, the nervous system. Tumours are vascular but nerveless. The free life of tumours is best seen in the cancers and sarcomas. A periosteal sarcoma will invade and utterly destroy by its increase first the bone in which it has arisen and then the whole organism. And at the other end of the scale of tumours, this freedom from organismal control is also shown. Large fatty tumours may exist in emaciated subjects. Sir James Paget speaks of a specimen "of considerable size in the mesentery of a patient from whom in the extremest emaciation of phthisis, nearly all the natural fat was removed."*

Here, then, we meet with something in which a tumour is distinctive. This single quality of self-dependence sharply marks off new growths from ordinary growth, hypertrophy

* Lectures on Surgical Pathology, p. 376.

and repair. What can be its meaning? The answer to this question has ever been the crucial test of the sufficiency of former hypotheses of tumour-disease, and it now devolves upon us to furnish an answer.

§ 3. *Explanation of the Self-dependence of Tumours: Neoplasia identified with Genesis in the Protozoa.*

We began by assimilating tumour-formation to the formation of tissue observed in ordinary growth, hypertrophy, and repair. The former and the latter have this in common that the elements of growth are derived from the cells of the tissues and the process of growth is by cell-divisions. Tumour-formation and tissue-formation are both, then, forms of organic increase. Now in the world of living things all forms of increase may be placed in one or other of two great categories. The increase is either continuous or discontinuous. Continuous increase is what we call growth (ordinary tissue-formation, hypertrophy, and repair), and discontinuous increase is what we call genesis (the reproduction of new individuals). Of these two modes of organic increase probably the oldest ontogenetically is that discontinuous increase exhibited by simple unicellular organisms, and from it, it is believed, the continuous form (growth) has been derived. It is now an accepted datum of evolution that the primordial form of organic increase is the generative process shown us by the lowest living creatures. These, of the natural orders Protozoa and Protophyta, are unicellular bodies, and multiply by cell-divisions analogous to the cell-divisions by which multicellular organisms (Metazoa and Metaphyta) add to their masses. But the new cells of Protozoa and Protophyta, as fast as they are generated, are dispersed in the form of discrete and independent organisms. Yet out of fortuitous clusters of these simple cells it is highly probable all the compound organisms were evolved. Sometimes mere mechanical impediments to separation will lead to temporary aggregations. This we see in Helizoa and Mycetozoa where, after multiplying by fission, the cells collect as an "aggregation-plasmodium." "A very

considerable number of infusorial animalcules foreshadow or typify in either their isolated or socially aggregated condition the separate or associated cellular elements out of which the higher tissue-structures or Metazoic organisms have been built up.”* Also with the rapidly multiplying Proto-phytes “their rapid multiplication sometimes causes crowding. When instead of floating free on the water they form a film on a moist surface, or are imbedded in a common matrix of mucous, the mechanical obstacles to dispersion result in a kind of feeble integration vaguely shadowing forth a combined group.”† Such chance unions were probably the first step in the evolution of the Metazoa, and by gradually increasing integration and differentiation of the, at first, feebly coherent cells there were ultimately reached those completely organized aggregates which are exemplified by all animals higher than the Cœlenterata.

It will now be understood, then, that what we call growth in the Metazoa is a repetition of the process of increase in Protozoa so modified as to have become continuous. “Asexual reproduction is simply discontinuous growth. . . . as we make an ascending survey of the Metazoa, that simple form of discontinuous growth which we term asexual reproduction becomes more and more subordinated to, and at last replaced by, that more differentiated or ‘sexual’ form of reproduction characterized by the union of two heterogeneous cell elements never to reappear save in degenerate forms.”‡

It ensues, therefore, that the discontinuous increase of Protozoa is at once the simplest form of growth and a form of genesis or true reproduction, and *it is to this that we may liken the generation of a tumour*. The protoplasmic bodies liberated from the normal tissue-cells, and which, after multiplying, appear as tumours, are, in relation to the normal tissues, centres of discontinuous growth. A tumour, as we have seen, is com-

* W. Saville Kent: A Manual of the Infusoria, v. 1, p. 99.

† Spencer: Principles of Biology.

‡ Encyclopædia Britannica, 9th Ed., v. xx. p. 407. Cf. also Geddes and Thompson: The Evolution of Sex.

posed of emancipated cells acknowledging no allegiance to the organism save that it is their means of nourishment. They are like the discrete, or mechanically aggregated, cells of Protozoa individual and independent. They are also produced as are Protozoa, by asexual multiplication. But the comparison is something more than one of mere resemblance as to particular traits. *The generation of a tumour must be regarded as a reversion to an ancestral mode of reproduction; as the resumption of a habit proper to the remotest ancestors of the Metazoa—the Protozoa. It is a seeding of the natural plastids of the body. As reproduction for the entire individual is effected by organs—ovaries and testes—specialized for the purpose, reproduction for the individual units is accomplished by the units themselves.*

§ 4. *The Conditions of the Genesis of Tumours: Histogenic Dissolution.*

Let us not attempt to advance without a momentary retrospection. Thus far we have decided that tumours are extended portions of normal parts, and are generated by the division of the protoplasm of normal cells. They also increase in mass as normal parts do by the multiplication of their units of composition, and while showing these traits in common with natural growth, hypertrophy, and repair, they are peculiar in an important way. Tumours are exceptional in the power of autonomous growth and development, being functionally and structurally uncombined with the rest of the organism. We have essayed to explain this characteristic by affiliating neoplasia to the discontinuous multiplication of unicellular organisms and regarding it as an ancestral reversion. But there is another and more important consideration to take part in our explanation of the self-dependence of tumours. It has to be disclosed that not only is neoplasia identical in process and product with an archaic form of genesis and growth, but is identical also in its determining conditions or circumstances.

There are numerous observations which, taken collectively,

establish the induction that one of the features of reproduction in the lowest forms of life is its association with the closing phases of vital action in the parents. Primitive types, both of plants and animals, evidence by the concomitants of the act of reproduction that among such creatures the division into offspring is frequently coincident with parental death. The cases are numerous, though the phenomenon has attracted little attention, where, as progeny are produced, the parent form vanishes. A good example is the spore-formation of micro-organisms. If we take the common hay-bacillus (*Bacillus subtilis*), the adult creature is observed to be a slender rod of protoplasm, which may exist singly or united with others as a chain or thread. Reproduction here is either by simple fission of the rods or by the formation within the substance of the rod of spores or seeds, but the formation of spores is always accompanied by the disappearance of the parent; the substance and the life of the adult bacillus are wholly resolved into offspring. "The spore grows at the expense of the protoplasm of the cell, which in time, together with the cell-wall, entirely disappears."* On germinating, the spore, which is an exceedingly minute speck of protoplasm, assumes the form of the parent. The same phenomenon is seen in Diatomaceæ. Here, also, "the old individuality disappears either in the swarms of zoospores it dissolves into, or in the two or four new individuals simultaneously produced by fission."†

Among animals a resolution of the parental protoplasm into the germs of a fresh generation may be witnessed in Gregarina and some Infusoria. "A spontaneous breaking up of the body occurs in some Infusoria. It is of normal occurrence in the multinucleate Opalina, where it leads to the formation of new individuals."‡ "The gemmules of the common fresh-water sponge are formed in the decay of the asexual adult, while even the sexual summer forms, especially

* Crookshank: Manual of Bacteria.

† Spencer: Principles of Biology.

‡ Saville Kent: Op. cit.

the males, are peculiarly unstable and mortal.”* And even in some primitive annelids (*Polygordius*) the mature females perish with the liberation of ova.

Sometimes it may be seen that this kind of genesis is hastened by circumstances which shorten the term of parental life. Innutrition and oxydation are capable of bringing the lives of micro-organisms (bacilli) prematurely to a close, and under these circumstances the organisms are transformed into young cells (spores) endowed with the power of new life.† Similarly with the microbic *Algæ* of sulphurous waters; as the sulphur consumed by these creatures diminishes they become motionless and break up into spores. *Mucor mucedo*, one of the moulds, likewise, when multiplying by oospores, does so only when the life of the fungus is waning; and if the liquid in which yeast flourishes, dries up, multiplication by budding is arrested, and the protoplasm of the cells is resolved into endogenous spores.‡ In a ciliated infusorian (*Leucophrys*), “so long as food is abundant, fission obtains; but when food grows scanty, there is a metamorphosis without encystation, followed by six successive divisions.”§

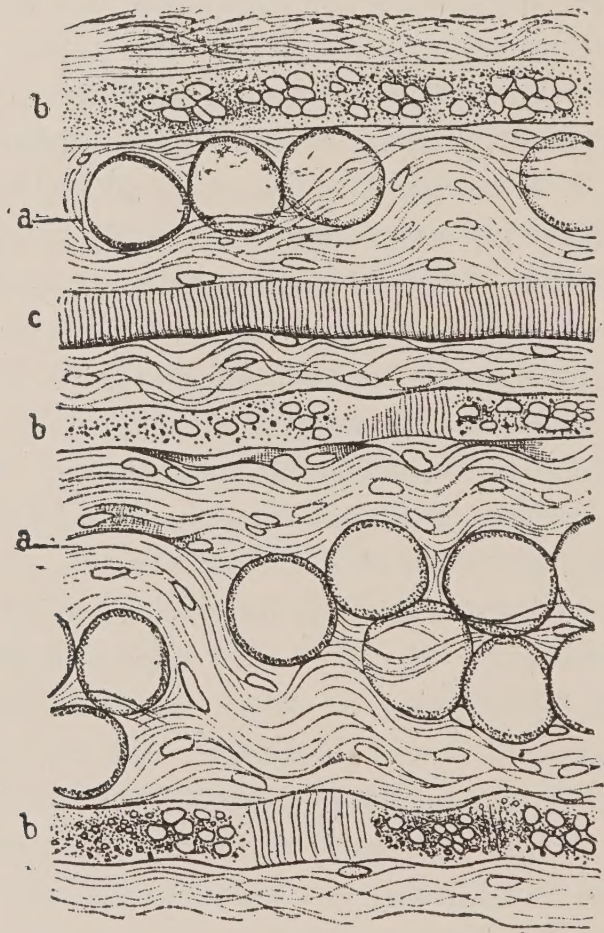
This primordial trait has left its mark even upon the highest plants and animals. If the flow of sap in still-growing trees is diminished by ringing or other injurious action they will cease to grow and begin to flower. In the shape of buds reproductive centres may be induced in bulbs by cutting out the embryo. The aphis, kept in an artificial summer, may for years be made to reproduce by parthenogenesis, but with want of food or a low temperature sexual genesis will set in. Similarly with the common *Hydra*. A vestige of the trait probably remains even in man where death is often accompanied by the ejection of seminal fluid. In man, however, there may be witnessed in the cellular units of his body not merely a suggestion of this association of life and death but the actual

* Geddes and Thompson: *Op. cit.* † Klein: *Micro-organisms and Disease*.

‡ Trouessart: *Microbes, Ferments, and Moulds*.

§ Geddes and Thompson: *Op. cit.*, p. 235.

phenomenon as exhibited among the Protozoa. Varied forms of disease are attended by a discontinuous multiplication of cells concomitant with the destruction of tissue. In acute neurotic muscular atrophy the nuclei of the muscle corpuscles sometimes multiply so abundantly as to fill the sarcolemma, and the adjoining figure (Fig. 1) serves to show that with the



(Figure 1. after Hayem.) Infantile Paralysis.—*a a*, Excess of connective tissue, containing a large number of connective tissue and fat cells ; *b b*, atrophied muscular fibres, containing a large number of nuclei; *c*, simple atrophy of muscular fibre.

process of reproduction the muscle tissue as such has ceased to exist. All that is special and distinctive of muscle has given place to an assemblage of simple cells and granules. The same thing is seen in Wallerian degeneration of nerve, and probable in some inflammations associated with degeneration.

Of the parasite *Trichina spiralis* it is said "they produce considerable destruction by piercing the sarcolemma, and disintegrating the sarcous substance, and there is often to be found a germination of the muscle nuclei around the worm."* Giant cells sometimes afford an illustration, as when they are degenerated at the centre and proliferate at the margin. And in karyokinesis observers have noted that the nuclear division may proceed step by step with the dying of the cell.

This phenomenon of reproduction in simple cells conjointly with the effacement of the parent form, I propose to distinguish as HISTOGENIC DISSOLUTION. Our conceptions of it would be clarified and enlarged by considering its broad relations to other forms of asexual and to sexual genesis, but this would involve an embarrassing digression and we must be content here to perceive its significance and then make of it the intended application.

The facts that have just been advanced declare most plainly that the underlying and precursory condition of histogenic dissolution is the oncoming of death in the parent. It is not the multiplication of new centres which antecedes and leads to the disappearance of the individual cell but the impending termination of individual life which leads to multiplication. The cessation of individual life may come in natural course as we see in Diatomaceæ and Infusoria; it may be accelerated by circumstances of food and oxydation as we see in micro-organisms, algæ, and infusorians; or it may be accelerated by injurious actions as we see in disease; but in every instance the dissolution of the parent with the formation of progeny is related to the approaching end of the parent. It is shown that, in cells, either separate or compounded into complex organisms, as the individual cell-life is drawing to a close there is a disposition to increased activity of the functions which subserve the life of the species. The current interpretation is, that such reproduction is a final effort of the individual to preserve the race, and doubtless this expresses a

* Coats: Manual of Pathology.

truth. Elsewhere, in endeavouring to account in mechanical terms for this fact of histogenic dissolution, I have remarked that during the evolution of Protozoa and Protophyta this tendency to dissolve into germs before life ceased altogether would so promote the continuation of the species that, appropriated by natural selection and perpetuated by heredity, it would become deeply stamped in the constitution of the units of compound organisms. Reproduction as an attribute of protoplasm is probably almost as fundamental as nutrition.

Looking a little more narrowly at the conditions of histogenic dissolution we become aware that it must arise out of a state of the cell-protoplasm not accurately denoted by the term "death." Before division sets in the cell contains a store of vitality otherwise the production of offspring would be impossible, but the store is a diminished one. Death is not actual but impending. It would appear that when the contained energies of the cell are insufficient to maintain the balanced functions needful for individual life, the remnant of contained energies being equal to the less costly function of reproduction is consumed in a last effort to continue the species. So that a necessary condition of histogenic dissolution is a more or less *gradual* decline of life in the individual cell. Sudden and complete death is obviously as incompatible with this form of reproduction as with any other.

And now to make this undeniable fact of use in our hypothesis. It is here assumed that out of centres produced by histogenic dissolution tumours originate, grow, and propagate themselves. It is assumed that the units of our bodies are the descendants of once discrete cells, and that amid all the changes of evolution they have retained in latent form some of the elementary traits of their Protozoan ancestors. One of these traits is the mode of reproduction by a resolution of the parent protoplasm, and having as its condition the ebbing of parental life. In tumour-disease the latent capacities become actual. Under circumstances inimical to the continued life of the cells of the tissues, these cells revert to an archaic form of multiplication, and the new generation

thus set free draw nourishment from the body, and grow by the processes of ordinary growth into the substance of a tumour. Thus, the most general and invariable condition of tumour-genesis is the dissolution of pre-existing tissue accompanied by the birth of tissue—not the condition, be it most carefully observed, of tumour-*growth*. The genesis of a tumour is one thing and the growth or increase of its mass is another. The processes are distinct in character and different, often quite opposite, as to their conditions. Let us compare more completely than was possible in § 2 tumour-formation with ordinary growth, hypertrophy and repair. Beneath the superficial difference that tumours are self-dependent, there is a deeper one. Tumours are the outcome of approaching death; but normal growth, hypertrophy, and repair are the outcome of a good reserve of vitality. The cells of the body, in normally multiplying to increase its substance or to replace lost parts, are not themselves effaced concurrently with the process of multiplication, but, according to our hypothesis, they *are* effaced in the genesis of a tumour. If upon the basement membrane of a mammary acinus there be a single row of secreting cells, and these cells divide to form a second row, as in normal growth, the primary or mother cells remain as before the process of division. But if, now, instead of multiplying for ordinary growth this row of secreting cells multiplies to form the cells of, say a cancer, the old individuality is obliterated. In the former case, it will be perceived, the nutriment contained in the blood, and in the latter case the substance of the mother tissues, is used to make offspring. The tissue having in this way given birth to the germs or embryonic elements of a tumour, these elements are free or segregated, and now begin to absorb nourishment from the blood and surrounding parts and themselves multiply by the processes of ordinary growth. Thus a neoplasm is like an ordinary growth or hypertrophied part in that its elements are derived from the tissues; it is like them in that its elements increase by the same process and by the same nutritive means; but it is unlike them in that the first elements or

embryos of the new growth follow on the extinction of those co-ordinating energies in the protoplasm, by whose means the structures and functions of the original cell are maintained. From this cardinal and covert difference arise the differences forced upon our observation by the behaviour of tumours—their self-dependence, their reproductive autonomy, and their antagonism to the organism. We are somewhat at a loss for suitable phrases to denote precisely the state of cell-protoplasm which is auspicious for histogenic dissolution. Hereafter, we shall speak of “exhaustion of tissue vitality” and “depletion of the vital forces,” &c., as leading to tumour-disease; but it should be understood at all times that what is meant is a failure in the powers of protoplasm to carry on the activities required for individuation as contradistinguished from the activities required for reproduction. Neither “exhaustion” nor “weakness,” nor any other term, can legitimately be used to express this state of things.

§ 5. *The Resistance of the Organism to the Growth of Tumours.*

This sketch of our hypothesis of tumour-disease is not yet complete. A very necessary component remains to be filled in. When the germs of a tumour have been generated in the manner we have supposed, it is manifest that the tissues will offer resistance to their increase. A tumour, whether of the benign or malignant class, is a decided detriment, for it draws its nutritive supply from the organism, but in return adds nothing to the sum of the organism's useful activities. Between the elements of a tumour and the elements of existing tissues there is, indeed, a continuous struggle for existence. In subsequent chapters we shall meet with many interesting examples of this, and often we shall be able to discern the circumstances which decide the issue of the conflict. For the present it will suffice to state the most constant of these circumstances, and here we touch a point in the general consistency of our hypothesis of an exceedingly striking character. The formation of a tumour is contingent on the inability of the tissues to compete successfully for

nourishment with their offspring. Note, now, that this contingency is supplied in large part by the very condition we have postulated for the genesis of tumours. *It is because the germs of a tumour are begotten by tissues whose vital powers are nearly exhausted that the germs acquire ascendancy.* The young have the prepotency of youth, and, by the hypothesis, are produced at places where the tissue life is declining; hence at these places the tissues have such feeble powers of assimilation that to a greater or less extent they yield to their relatively stronger parasitic progeny. If it were the case, as surface appearances have hitherto led men to believe, that a tumour signifies abnormal tissue-vigour—excess of vitality—the overthrow of the organism, or any portion of it, by a new growth, would mean the overthrow of a greater power by a lesser one. I think we shall find it indicated by the facts, when we come to examine them, that the growth of a tumour in any part is not solely determined by histogenic dissolution of some one or many of its units, but by the general vitality and resisting power in those surrounding units of the parts not actually involved in the dissolutional process. As we have seen, a multiplication of new centres with the disappearance of the old is the accompaniment of diseases not attended by the growth of tumours. Here, there will be found reason to think, the powers of normal life in the contiguous tissues are sufficient to prevent the multiplication of the germs set free.

§ 6. *Recapitulation and Conclusion.*

It will be recalled that this conception of tumour-disease applies to the whole series of simple- and compound-tissue tumours. Alike for the most innocent fatty tumour and the most malignant cancer, there is conceived a parentage in the natural tissues of the body; and in all, the process by which tumours are generated by the tissues is a process of asexual genesis conditional upon the decline of tissue-vitality. It follows, in effect, from what has been said that a true understanding of neoplasia and its relations to other forms of

organic increase lies in a perception of the change that takes place in the tissues at the moment when the embryonic tumour is produced. This change it is which constitutes the essence of neoplasia and gives rise to the specific characteristics of tumours. If our purview includes only the phenomena of growth in tumours their peculiar phenomena remain unexplained, and the phenomena they exhibit in common with growth, hypertrophy, and repair are equally uncomprehended.

From this hypothesis we must draw the corollary that a tumour is a local disease; local by the derivation of its elements, and local by the conditions of the derivation. Whatever the systemic or constitutional effects of tumour-disease, these are secondary, and not primary events. Nevertheless, although a tumour is local by origin and by cause, we shall find hereafter that constitutional or systemic conditions are not without influence both upon the genesis and the growth of tumours.

The task now will be to inquire whether this roughly outlined hypothesis will break down under the strain of facts or will be consolidated, and at the same time expanded by them. We must first confront it with the body of data which the microscope has revealed in connection with the morphology of tumours.

CLASSIFICATION OF TUMOURS.

1. MESOBLASTIC.

A. *On the Type of Embryonic Connective Tissue.*

The varieties of Sarcoma.

B. *On the Type of Fully-developed Connective Tissues.*

Representing fibrous tissue	Fibroma.
„ mucous tissue	Myxoma.
„ fatty tissue	Lipoma.
„ cartilage	Chondroma.
„ bone	Osteoma.
„ lymphoid tissue	{ Lymphoma. Lymphangioma.

C. *On the Type of Higher Tissues.*

Representing muscle	Myoma.
„ nerve	Neuroma.
„ blood vessels	Angioma.

II. EPIBLASTIC AND HYPOBLASTIC.

A. *On the Type of Embryonic Epithelial Tissues.*

Representing surface epithelium	Epithelioma (Cancer).
„ glandular „	Carcinoma „

B. *On the Type of Fully-developed Epithelial Tissues.*

Representing surface epithelium	Papilloma.
„ glandular „	Adenoma.

CHAPTER II.

THE FACTS OF MORPHOLOGY.

The Embryology of Tumours.—The Structural affinities of Tumours and the Tissues.—The Mixed Characters of Individual Tumours.—The Contiguity of Tumours to the Tissues they Represent.—The Relations of Tumours to Surrounding Parts.—Interpretation of these Relations.—The Modes of Tumour-growth.—Summary of the Morphology of Tumours.

§ 7. *The Embryology of Tumours.*

A separate chapter will be devoted to the secondary phenomena of tumours, so it should be continuously borne in mind that primary tumours still engross our attention.

If tumour-disease is really connected with the biological fact of histogenic dissolution (§ 4), it is a very pertinent question to ask whether there are any direct observations upon the beginnings of neoplasia that may be pointed to in evidence. There are a few such observations. Within these three or four years the actual conversion of gland cells into cancer cells has been witnessed and described by several observers. The latest of these observations with which I am acquainted are by Dr. D. J. Hamilton and Dr. J. Williams. Dr. Hamilton* thus describes the genesis of mammary cancer. "When a cancer is about to commence growing the epithelium within the acini begins to proliferate and distends them as represented in Fig. 154. As yet, however, it is still confined within the acini, and thus keeps up the gland character of the growth. The tumour is as yet an adenoma." I here reproduce two figures from Dr. Hamilton's work (Figs. 2 and 3), and direct the reader's attention to one of the facts they teach. Fig. 2, delineating the genesis of cancer from mammary acini,

* Text book of Pathology, vol. 1, 1889, p. 403.

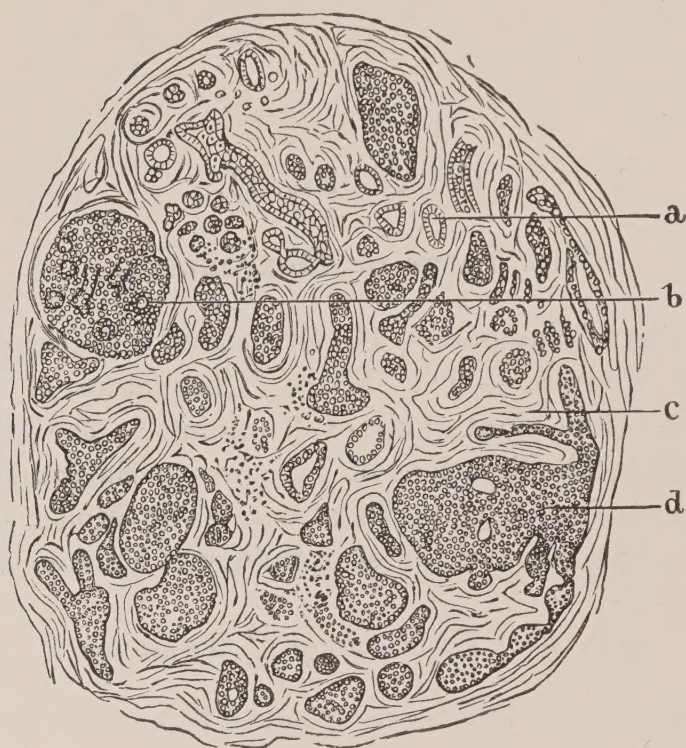


Figure 2 (Hamilton). Development of a Cancer of the Mamma. Lobule of the Gland in which the acini are in the Adenomatous stage ($\times 50$ diams.).

(a) Normal acinus; (b, d) acini distended with epithelium; (c) surrounding stroma.

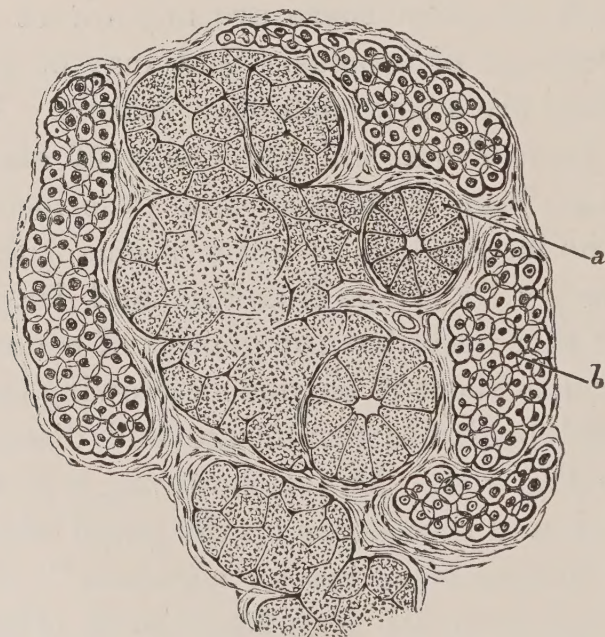


Figure 3 (Hamilton). Adenomatous stage of a Cancer of the Submaxillary Gland ($\times 350$ diams.).

(a) Section of a normal acinus; (b) an acinus distended with proliferating epithelium. Other parts of the gland were completely cancerous.

shows acini in various stages of transformation. There is a normal acinus (*a*) with a single layer of regularly-arranged columnar or polyhedral epithelial cells and there are acini (*bb*) filled to different degrees of distention with roundish cells more or less irregularly-arranged. Now the point to be specially marked,—is the disappearance of the original regularly-arranged epithel-

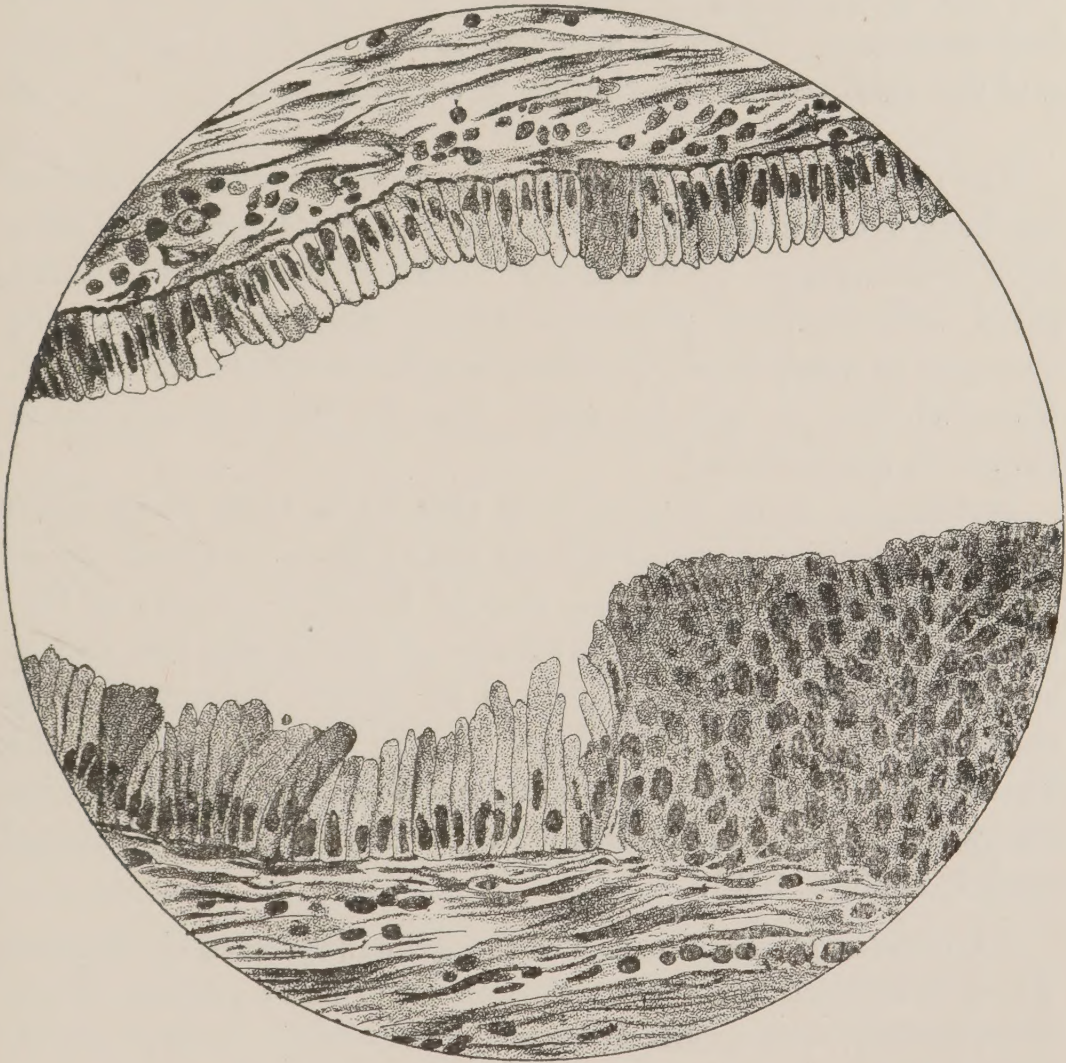


Figure 4 (Williams). Cancer of the Uterus.

ium from the converted acini. The substituted cells are greater in number, they are altered in character, and are disarranged, often being quite detached from the basement membrane. The appearances correspond exactly with expectation, if in the genesis of a tumour the elements of normal tissue are resolved into broods of young cells.

Fig. 3 also exhibits, in cancer of salivary glands, these features of the process of transformation. The change from the large pyramidal cells to small round cells is most striking.

In the work by Dr. Williams* may be seen many illustrations of the stages of transition of cervical mucous glands into cancerous foci. One of these (Fig. 4) shows one half (left) of the side of a gland with still normal epithelium, and the other half cancerous. Here the structure is seen under a high power, and the character of the change is very distinct.

The direct development of tumours from pre-existing tissues has been determined for nearly every variety of cancer. It has been demonstrated by Waldeyer† in cancer of the skin, clitoris, penis, sub-maxillary glands, stomach, and other parts with changes, in many cases, precisely similar to those here figured. (See Taf. viii. xi. xii., loc. cit.) Also by Birch-Hirschfeld in cancer of the testicle.‡

But of the many observations that have been made upon the tissue-origin of tumours none that I have met with are so striking and to the point as that of Dr. G. F. Cooke of Birmingham upon the actual conversion of gland cells into cancer cells in a case of primary cancer of the liver. Specimens from this case were exhibited by Dr. Cooke at a meeting of the Pathological Society of London, on May 1st, 1888, and the following is the report published in the *British Medical Journal* (vol. 1, 1888, p. 959).

“A microscopic examination of the growth revealed appearances which illustrated one mode of origin of primary growths in the liver, namely, from proliferation of the liver cells. Groups of cells were to be met with in the advancing part of the growth, which had very large nuclei, some of which might be observed to be dividing; in other parts a more active division of nuclei might be observed, and the various stages of karyokinesis. With this nuclear division, vacuolation and even division of the liver-cells

* Cancer of the Uterus.

† Die Entwicklung der Carcinome; Arch. f. Path. Anat. Bd. 41, 55.

‡ Zur Entwicklung des Hodenkrebses: Arch. d. Heilkunde ix. p. 538.

itself occurred, and thus at the margin of the small nodules of growth, columns of liver cells were formed in which both processes were going on. The bridges between the vacuoles finally became absorbed, while the nuclei became arranged at the periphery ; in this way a column of liver cells was converted into a tubule lined by a highly-nucleated protoplasmic border, or even filled with proliferating epithelioid cells ; a tubule thus formed, spouted in all directions, the nuclei at the same time rapidly proliferating, and thus the adenoid structure was obtained. The stroma of the growth was, Dr. Cooke believed, derived from the perilobular and intercellular connective tissue."

If the plate accompanying Dr. Cooke's paper in the thirty-ninth volume of the Pathological Society's Transactions be examined, the process of multiplication in the liver cells will be seen to correspond to histogenic dissolution.

Though these observations have as yet been only incompletely verified, we shall bear in mind in accepting them that Dr. Cook's statements are apparently uncoloured by any traces of the present hypothesis of neoplasia. I do not think it will be unsafe to see in the phenomena described direct and positive evidence, as far as it goes, of the origin of tumours by histogenic dissolution of the tissues.

An almost equally instructive observation, which we may consider confirmatory of Dr. Cooke's, has been made by Dr. Coats upon a case of primary cancer of the kidney—an organ like the liver of hypoblastic origin. "To the naked eye it is as if a portion of the kidney were transformed ; and with the microscope it can be seen, at the margin of normal and pathological, that the tumour is advancing by a conversion of the proper kidney tissue. The epithelium of the tubules is multiplying so as to form the cancerous epithelium, and is becoming irregular in form, while the cancerous stroma is being formed of the connective tissue of the organ."*

These instances of tumour-genesis do not unfortunately,

* A Manual of Pathology. American edition, p. 659.

in every case, furnish us with the nicer details of the process of cell-division. The respective shares taken by the nucleus and the protoplasm of cells at the moment of dissolution remain undetermined, and we are left to infer from the results the general character of the changes. What were once definite and organized structures, have clearly given place to relatively indefinite and unorganized structures; but the process of transformation is much a matter of inference. There must, however, be difficulties in detecting *post mortem* the steps of the process if it is concomitant and conterminous with the process of individual death. It seems probable from Dr. Cooke's observation, and the characters of embryonic tumours, that nuclear division forms a part of the process of dissolution. That tumours *grow* by nuclear division is now an acknowledged fact.* Indirect division (karyokinesis) has been seen in an actively growing cancer of the mamma, and in sarcomata.† Growth in a spindle-celled sarcoma is thus described. "The nucleus of a particular cell is noticed to become enlarged and, subsequently, slightly constricted in the middle, so as to assume a dumb-bell shape. A similar depression is noticed in the body of the cell. The nucleus completely divides into two, while the indentation of the body of the cell becomes deeper, and the junction between the two halves more attenuated and drawn out. Each nucleus retreats into a half of the cell, and the separation between the two parts of the body shortly becomes completed, two new spindles thus resulting."‡ Now, having regard to the hypothetical parentage of tumours, and the hypothetical affinities of the tissue cells with unicellular organisms this fact of the growth of tumours by karyokinesis is important. In ordinary tissue growth the process is by karyokinesis, and the same kind of multiplication obtains among the lower animals and plants.§ Radiolaria and Fora-

* Ziegler: Text-book of Pathological Anatomy and Pathogenesis. Translated by Dr. MacAlister, § 139.

† Hamilton: Op. cit. vol. 1, p. 355.

‡ Ibid. p. 366.

§ Strasburger: Ueber Befruchtung und Zelltheilung. Peremescho: Arch. f. Mikrosk. B. xvi.-xvii. Fleming: Arch. f. Mikrosk. B. xvi. xviii. xx.

minifera show multiplication of the nucleus preceding the resolution of the protoplasm.* Nuclear division has also been demonstrated in segmentation of the ovum, in normal regenerations, and in most pathological cell-formations.

It may be urged of the facts cited in connection with the genesis of cancer that they prove nothing as to the genesis of sarcoma and the benign growths; they speak only of the origin of cancer cells. Why is there not at hand similar evidence in the case of the innocent tumours and sarcoma? One of the reasons for this absence of evidence where it might naturally be looked for is, perhaps, the prevalence of certain doctrines. Many pathologists think that tumours are due to the growth of embryonic rudiments; some think they are deposited from the blood; but comparatively few trace them directly to the tissues. Another reason is the fact that innocent and malignant tumours are not generated under quite identical circumstances. At a later stage it will be shown that a cancer is the expression of a deeper and more extensive tissue degeneration than is any innocent growth. Often considerable tracts of tissue, as in the case quoted from Dr. Coats's "Manual of Pathology," will undergo simultaneously or in quick succession the conversion into cancerous structure. But in the benign tumours the beginnings are usually exceedingly small. A very limited group of tissue-cells divides into the germs of a tumour, and when these germs have grown into a visible and often highly organized mass all signs of the process by which the mass was started have been wholly erased. Therefore the scarcity of evidence on the point in question is not to be wondered at. There is, however, in the embryology of tumours indirect evidence that all new growths, both innocent and malignant, proceed from histogenic dissolution of the tissues. In the early stages of their development the cells of tumours possess structural characters according completely with this idea. Tumours of mesoblastic tissue—those of the

* Rolleston: Forms of Animal Life.

connective-tissue type—begin as minute masses of undifferentiated protoplasm. No matter how complex and complete in structure is the mature growth, it starts as a congeries of the simplest units. The first product of the neoplastic change is “a new issue composed of small roundish cells, from $\frac{1}{1800}$ th to $\frac{1}{2500}$ th of an inch in diameter, enclosing a large ill-defined nucleus. These possess no limiting membrane, but are simply little masses of amœboid protoplasm, lying in a scanty, semifluid, and faintly granular intercellular material. This tissue is precisely similar to embryonic tissue. It would be impossible to determine at this stage of the growth what it will ultimately become—whether a fibroma, a sarcoma, or an enchondroma, &c.”*

The following description of the mode of extension in cancer of the rectum depicts the characters of embryonic tumour cells. “If a section be cut through the new growth, extending into the healthy submucous tissue, it will be seen that there is a kind of no man’s land intervening between the growth and the normal tissue. This is infiltrated with a cloud of cells.

“The cells forming the extreme border of this infiltration differ in no way from ordinary lymphoid cells, but as they are traced towards the growth they are seen gradually to become larger, and to assume a distinctly epithelial type. These in their turn gradually assume the appearance of an ill-marked adenoid tissue, which in time assumes a more definite type.

“In short the appearances suggest that the growth increases by the gradual conversion of the lymphoid cells on its border into adenoid tissue, and that the source from which these lymphoid cells are derived is the epithelium of the growing tumour, a portion of them gradually developing into the likeness of their parents causing the extension of the growth.”†

* Green : Pathology and Morbid Anatomy, 6th ed., p. 115.

† Harrison Cripps : Diseases of the Rectum and Anus, 2nd ed., p. 363. See plates iv. xi. and xii.

The growing edge of a tumour of epiblastic tissue, say an epithelioma of the tongue or scirrhus of the mamma, also shows this indifferent tissue. So simple and so much alike are the embryo cells of tumours that it is often impossible to distinguish the cells of sarcoma from the cells of cancer, and in some cases the simplicity of the cells is such as to approximate them to creatures as low in the scale of life as micro-organisms; witness the following description of cells in a case of multiple sarcoma. "The pleura was considerably thickened by an infiltration of small round cells, which were closely packed together. These small cells varied in size; but they were all small, and like those described as composing a large portion of the mediastinal growth. Many had very little cell-substance, the chief part being nucleus. These cells retained the aniline dye very tenaciously, just like micro-organisms, when the sections were treated according to Gram's method. They were, however, not micro-organisms."* And in a case of scirrhus of the mamma in a woman fifty-eight years old, Dr. Creighton describes the cells "as little else than nuclei without cell substance."†

When tumours form upon the external surface of the body, the naked-eye changes in the tissues may sometimes be readily observed. Scars are extremely liable to cancerous change. "When a scar commences the onset of the evil, it may often be noticed at one point to become thinner, a little moisture escapes, and a scab and sore become established. At other times one or more small tubercles raise up the scar, and, breaking through, coalesce to form a kind of warty growth . . . On an open sore, where there has simply been for so long a smooth, unhealing surface, granulations spring up in some one spot, and, spreading gradually, cover its entire extent." When moles are about to become sarcomatous (melanotic sarcoma) "it is observed generally that the spot where it is situated has become slightly hardened or increased in size,

* Harris: Medical Chronicle, vol. ix. no. 5.

† Tumours of the Breast.

that the ordinary colour of the mole is disappearing, and that on its surface, or near to it, there is a tendency to the production of discharge and very slow ulceration. . . . In some instances an evident growth appears to lift up the surface of the mole, tending in like manner, as time goes on, to the establishment of similar conditions.” *

These observed characters of the tumour-units at an early stage of their existence, and in growths that remain embryonic, are just what might be expected if neoplasia is a “seeding of the natural plastids of the body.”

§ 8. *The Structural Affinities of Tumours and the Tissues.*

From the embryology of tumours we pass to groups of facts connected with the morphology of adult growths. It is now a common-place of morbid anatomy that “every pathological growth has its physiological prototype.” Each tumour can be referred to as representing this or that tissue. In the connective tissue series there are representatives of fibrous, mucous, and fatty tissues; of cartilage, bone, muscle, and nerve; of lymphoid tissue and of blood-vessels. In the epithelial group, representatives of surface epithelium, papillæ, and glands. The former constitute the species fibroma, myxoma, lipoma, enchondroma, osteoma, myoma, neuroma, lymphoma, and angioma; the latter the cancers, papilloma, and adenoma.

Of these species there are many varieties whose morphological relationships are mainly referable to the stages at which development ceases. We saw a moment ago that during the first stage of their life-history all tumours are alike in consisting of undifferentiated cells. Taking first tumours of connective tissue type, if development stops at the embryonic stage there results round-celled and melanotic sarcoma; if development is in advance of this, spindle-celled, alveolar, and myeloid sarcoma; while with full development

* Pemberton: Clinical Illustrations of Various Forms of Cancer.

there results the prototypes of fibrous, mucous, and other adult tissues.

Between the most embryonic round-celled sarcoma and pure fibroma, transitional forms are known which clearly register degrees of organization. Applying to them the criteria of organic development the round-celled sarcoma is but little in advance of the feebly integrated, homogeneous, indefinite particles of which all tumours at first consist. "It is an exceedingly soft tumour, often half-diffuent." Its cells are clustered with little connective substance; nor does round-celled sarcoma generally possess that integrated form resulting from the development of a capsule; they are commonly imperfectly delimited from the surrounding tissue. But in passing to the gliomatous, melanotic, spindle-celled, and myeloid varieties of sarcoma, the elements are seen to have advanced in integration, complexity, multiformity, and definiteness, and show an increasing resemblance to the tissues whence they were presumably derived.

Mr. Eve* has said of these transitional forms, they "are as potent as any anatomical fact can be in the connective tissue series, whether of the hard or soft parts. Fibrous tumours occur in every variety, from the dense compact nodules composed of parallel bundles of well-formed fibrous tissue to the soft and sometimes semi-gelatinous growths, which however are not malignant." From the fibro-sarcomata "we reach the spindle-celled and finally the round-celled varieties of sarcoma, in which the elemental round cell makes not the slightest effort in the direction of organization, not even to the formation of a spindle-cell." Biologically and histologically speaking, the distinction between the sarcomata and fibrous, cartilaginous and osseous tumours, is principally one of development, however wide their clinical differences.

When we turn to neoplasms originating in epithelial tissue, we meet with the same facts of structure. Encephaloid cancer

* British Medical Journal, vol. 1, 1886, p. 299.

is the counterpart of round-celled sarcoma, though not usually presenting quite the embryonic characters of soft sarcoma. It is remarkable for the want of union among its elements and the simplicity of its structure. "Encephaloid cancer is of soft brain-like consistence." "The proportion of its stroma is very small." And between the immature encephaloid cancer and scirrhus, or hard cancer, "there are all intermediate stages."* "Encephaloid and scirrhus cannot be regarded as in any way constituting distinct varieties of carcinoma." So, too, between the malignant scirrhus (gland cancer) and the benign adenoma, every degree of development is encountered. Sometimes in scirrhus of the mamma the acini are well-formed, and the neoplasm closely repeats the morphology of the gland. Adenomas frequently repeat precisely the tissue of glands; and adenomas of the mammary gland sometimes contain acini so advanced in organization as to produce milk.†

Again, epithelioma or cancer of surface epithelium, reproduces in different degrees the peculiarities of the epithelial tissue of the regions which are its common seats, and exhibits by individual development and the divisions of its class the morphological trait we have noted of other neoplasms. Writing of skin-cancer, Dr. Thin says ‡:—"In the natural evolution of an epidermic cell there are certain well-defined stages. The small cell in which the protoplasm stains deeply with certain colouring agents, and in which the nucleus more particularly is easily and deeply stained, may be taken as representing the first stage. The large, flat, horny cell, which does not stain deeply with carmine or logwood, and in which the nucleus scarcely stains at all, may be taken as the last stage. It is characteristic of certain stages of epithelioma that, in the new formation, cells representing both these stages, and all intermediate ones, are found throughout the growth."

Once more, flat-celled epithelioma of the mouth, pharynx, vagina, &c., is described in various stages of development of cells and stroma; it often grows outwards as does villous

* Green: *Op. cit.*

† Bryant: *Diseases of the Breast*, p. 160.

‡ *Cancerous Affections of the Skin.*

cancer, and approximates to the papillomata. And cylinder-celled epithelioma, as of the stomach and intestines, sometimes partakes of the characters of cylinder-celled glands.

How must we read these unquestionable truths—the truths that structurally tumours are copies of the tissues, and that development from indifferent cells is the key to the relationships of varieties? We must say, even if the facts are not in open conflict with a counter-hypothesis, that with the present hypothesis they are in complete keeping. If the various tissues reproduce themselves by asexual genesis, and the young cells have varying developmental powers, there should be just these likenesses and differences among tumours.

The object of this section has been to set forth the natural kinship of tumours and tissues as vouched for by their common morphology. We must not close, however, without any reference to the alien characters of some tumour-cells. The cells of a scirrhus cancer and those of some sarcomas are often quite unlike the normal cells. In carcinoma of the mamma we find cells of large size, of very various shapes, with unduly prominent, large, and numerous nuclei and nucleoli, differing in all these particulars from the cells of the natural gland. Formerly the recognition of these peculiarities led to the doctrine of specific cancer-cells; but at the present time we believe them not to be indications of specificity. The unlikenesses of structure are direct consequences of unlikenesses in the conditions of life. The large size of the cells of a scirrhus cancer are probably due to their unrestrained growth; their diversity of form to their modes of aggregation; and the multiplicity, largeness, and prominence of their nuclei and nucleoli to their unrestrained reproductive proclivities.

§ 9. *The Mixed Characters of Individual Tumours.*

We have just noted the relations which tumours exhibit when arranged according to the type or kind of tissue represented; and here we have to note that individual tumours very

frequently possess the characters of two or more varieties. Thus, a tumour may combine the elements which constitute fibroma and sarcoma, or fibroma and myoma. Myoma may exist in union with lipoma, sarcoma, chondroma, or adenoma. In osseous tumours there is often an admixture of sarcomatous elements. Among epithelial tumours, encephaloid and scirrhus, and scirrhus and adenoma, are met with in a single growth.

In many instances, the mixed characters of these neoplasms are readily explained if the common starting-point of tumours is an embryonic tissue with potentialities for development according to its parentage and powers. Certain parts of a tumour will remain embryonic, perhaps from local circumstances, while other parts become well organized; and thus there may be, for example, a combination of sarcoma and fibroma. "Sarcomas are very liable to organization, and large masses of tumour may be changed into fibrous tissue, bone or cartilage But there almost always remain some softer portions in which the sarcoma structure still exists."* A further cause of variegation is the common origin in the mesoblast of all the connective tissues—muscle, bone, cartilage, fat, &c. Then it is to be remembered that the normal tissues are made up of diverse elements. Glandular tissue or muscular tissue is never without connective tissue. In an adeno-sarcoma of the mamma, it is from the connective tissue that the sarcomatous elements are derived, and from the glandular tissue that the adenomatous elements are derived.

Some of the finer structural details of tumours may be referred to the qualities of tissues in particular situations. Thus the softness of glioma and the hardness of other fibrous tumours are due to the delicacy of the intercellular substance in the brain, and its coarseness in other parts.

Diversity in the structure of tumours sometimes arises from the presence in them of embryo-like substances. We have

* Butlin : Sarcoma and Carcinoma.

seen how in the first stage of their life-history tumours repeat the primitive tissue of the embryo. The simple homogeneous cell-masses of soft sarcoma, for example, are identical with the substance out of which are developed the adult tissues. Probably every tissue of the body is first laid down in amœboid protoplasm. Now, not only is there in tumours a recurrence of this most rudimental character, but we find, in several kinds of new growths, other embryonic structures.

In the foetal state many of the tissues consist of a soft mucin-yielding substance. Such is the substance of connective tissue in the embryo; and the umbilical cord and vitreous humour of the eye are instances of its persistence after birth. In the myxomata there may be observed a re-appearance of this immature or embryonic connective tissue. "The myxomata always originate from embryonic connective tissue, which does not advance beyond the mucous stage of normal development."* "Tumours are not unfrequent, especially in the parotid region, which are thus intermediate between cartilage and mucous tissue, so that we cannot say to which they most properly belong; also, many fatty tumours show clear gelatinous patches of mucous tissue in all transitions to fat, while some myxomata show opaque spots composed of true adipose tissue."†

In the variety of chondroma known as osteo-chondroma, the osteoid tissue resembles the osseous structure in rickets, where the changes are described as consisting of an "increased preparation for ossification but an incomplete performance of the process." The osteoid tissue of osteo-chondroma would be true bone were it calcified, and probably it answers to a stage in the normal development of bone.

According to Dr. Creighton, crude structures suggestive of the process of blood-formation in the embryo exist in some tumours, as in cystic sarcoma and cavernous angioma of the liver. This hæmatoblastic process is thus described in a case of cystic sarcoma: There were "spaces lined with cubical epi-

* Green: Op. cit. † Wilks and Moxon: Pathological Anatomy, 3rd Ed.

thelial-like cells. The surface row of cubical cells loosen from their attachment, fall into the space, and are succeeded by another row, which are detached in turn, and so the excavation proceeds at many centres. The detached cells do not remain free solid elements, they may sometimes change into a mucous fluid, but their full physiological activity is the hæmatoblastic or blood-making. The spaces contain the hæmatoblastic cells and their derivatives in various forms. One may see the cubical cells in the margin of the space acquiring a yellowish tint, then the same cells disengaged and lying free in the space and probably increased in size, then red-blood-discs of the same colour as the protoplasm of the hæmatoblasts, and cells with several nuclei corresponding to those already described as the surviving nuclei of the disintegrated hæmatoblast, the whole lying in the midst of a mucous like coagulum. This is neither more nor less than the early blood-making function of the mesoblast revived.”*

I think it must be admitted that these groups of facts evidence very cogently the community of nature between tumours and the different tissues of the body. As revivals of embryonic modes of tissue-life, the phenomena we have just noted are intelligible on the supposition that a tumour is the product of tissue-genesis. It certainly agrees with the inductions of embryology, that when the units reproduce themselves the new generation should tend to repeat the phases of their embryonic development.

A very interesting cause of variety among tumours is the generation of tumours by tumours. Adenomas of the mamma and condylomata frequently become cancerous; that is, the tumour cells repeat the genetic process of the normal mother tissues. And tumours of connective-tissue type—myomas, fibromas, and enchondromas—become sarcomatous. This fact is not only quite explicable by our present hypothesis, but is inexplicable by any other. Histogenic dissolution is just as

* Encyclopædia Britannica, vol. xviii., 9th Ed. p. 369.

intelligible a process in tumour-cells as in tissue-cells. Moreover, we shall subsequently see that tumours are very favourably conditioned for histogenic dissolution, for generating lower kinds of new growth. The change is called cancerous and sarcomatous degeneration, and, as far as our present knowledge extends, a tumour growing from a tumour is always of inferior type.

Lastly, the substance of tumours becomes diversified in consequence of ordinary degenerative changes. The degenerations proper to the normal tissues are common in neoplasms. We meet with atrophy, colloid, mucoid, fatty, calcareous, and cystic degenerations. The atrophy of glandular cells in scirrhus tumours and of muscle cells in uterine myoma is the cause, in many examples, of the varying proportions of parenchymatous and connective elements. Colloid cancer results from the conversion of cancer cells into colloid material. Cystic degeneration gives rise to a large and characteristic class of tumours whose anatomy is now well understood. The most common form is cysto-sarcoma of the mammary gland. In this the cysts are dilated gland structures (acini and tubules). From epithelial changes within the acini or from extra-acinous growth, the ducts or acini become obstructed and then dilated. The fluid contents of such cysts are often produced by the proliferation and subsequent liquefaction of glandular cells.

§ 10. *The Contiguity of Tumours to the Tissues they represent.*

We may next consider some facts respecting the seats of new growths. With remarkable constancy primary tumours grow from and are situated among the tissues they resemble. It will suffice to set down a few extracts from Dr. Green's "Pathology and Morbid Anatomy."

Of the sarcomata, it is said they always originate from connective tissue. The small spindle-celled variety grows from "the periosteum, the fasciæ, and connective tissue in other parts." The melanotic sarcomata originate principally in two

situations—in the choroid coat of the eye, and in the superficial integuments (warts and moles) where pigment is normally present. Osteoid sarcoma is “met with almost exclusively in connection with bone.” Lympho-sarcoma “may begin in lymphatic glands or in connective tissue elsewhere.” Myeloid sarcomata, containing myeloid cells found in the medulla, “nearly always occur in connection with bone and most frequently originate in the medullary cavity.” “Fibroma, myxoma, and lipoma also generally arise in corresponding tissues. Chondromata—tumours it will be remembered of connective-tissue type—are derived from common connective tissue and bone, very rarely from cartilage.” “The development of chondroma from connective tissue is precisely similar to the physiological process.” Osteo-chondroma “originate beneath the periosteum, their common seat being the ends of the long bones.” The formation of osseous tumours “may, as in normal development, take place directly from fibrous tissue or be preceded by the development of cartilages: thus we get fibrous and cartilaginous exostoses.” “Bony tumours are much commoner in connection with bone (homologous) than elsewhere (heterologous).”

“The lymphomata originate from lymphoid tissue, being simply uniform overgrowths of pre-existing lymphatic structures—mainly of the lymphatic glands. They may, however, be heterologous.” Non-striated myomata “probably always originate from muscle,” and the neuromata from pre-existing nerve tissue.

From pre-existing gland structures the adenomata always grow. And we may be sure that the congeners of adenoma, the carcinomata, are derived from the cells of glandular epithelium. Distinguished observers have, however, asserted that connective tissue may be the source of cancer cells. But we find invariably that each variety of cancer possesses characters corresponding more or less closely to the tissue from which it springs or to the structure of its primary. Thus the epithelial elements of cancer of the lip are of the squamous kind and mimic the squamous epithelium of the labial region;

the epithelial elements of adenoid cancer of the rectum are like the columnar epithelium of the gut; and scirrhous of the breast imitates the structure of that organ.

Though probably in every case the source of the elements of tumours may be traced to correspondent tissues, there remain some so-called heterologous growths that our present knowledge is insufficient to fully explain. Examples are the enchondromas of the testicle and parotid gland. Cartilage in such situations may be connected with existing fibrous tissues, but why neoplasms of the testicle and parotid gland should so frequently contain or consist of cartilage is still obscure. The muscular tissue found in congenital sarcoma of the kidney (rhabdomyoma) has been thought to take origin in the Wolffian body; an embryonic structure.

It must, however, be acknowledged that in an overwhelming excess of cases the observed seats of new growths are what we should anticipate if the latter proceed from a process of genesis in the natural structures. The very terms in which the foregoing observations are recorded appear like a conscious argument for the assumption that tumours are the direct descendants of the tissues.

§ 11. *The relations of Tumours to surrounding Parts.*

Neoplasms receive well-marked characters from their relations to surrounding structures. Some of the differences among new growths thence arising are of the greatest interest. They are of interest because immediately associated with them are the phenomena of innocence and malignancy in tumours; and they are of interest on account of their interpretation. Roughly speaking there are three ways in which tumours are connected with contiguous parts. Their substance may be continuous with the normal tissues, invading and permeating these; it may be separated from them by a capsule of connective tissue; or the tumours may be altogether external as in warts and polypi. With remarkably few exceptions the tumours whose elements are diffuse or blended with neighbouring parts are tumours of low organization. The embryonic growths in the epithelial

series (the cancers) are perhaps invariably diffuse. "Unlike almost every simple (benign) tumour, it (cancer) is not in any way encysted or encapsuled."* And the immature growths of the connective-tissue series are generally or often diffuse. Soft sarcoma is seldom circumscribed though the higher forms, as the spindle-celled and myeloid may be, and, perhaps, usually are, bounded by connective tissue or by bone. "They increase by the continuous invasion of their connective-tissue matrix, so that no line of demarcation exists between the two. They frequently invade also other tissues, the elements of the growth extending for some distance into the surrounding structures."† The softer or less completely developed forms of fibroma and chondroma are also sometimes more or less diffuse. The soft fibromata "are met with as diffused growths in the subcutaneous and submucous tissue."

Now, on the other hand, as the quotation above and those below testify, tumours representing the mature tissues are nearly always encapsuled. Adenoma of the mamma, for example, is an encapsuled growth, but not so an undeveloped adenoma or cancer of this organ. And capsules are the rule in fibroma, myxoma, lipoma, chondroma, osteoma, and neuroma. The firm fibromata "are hard encapsuled growths." Myxomata "are usually separated from the surrounding structures by a very thin capsule." Lipomata "are usually surrounded by a fibrous capsule which separates them from adjacent structures." Chondromata "are usually encapsuled, and in most cases produce merely local effects." Spongy osteomata "consist of cancellous, surrounded by a thin layer of compact bone." "A growing spongy exostosis is covered by a layer of cartilage; when this ossifies, growth ceases."

The tumours that are not imbedded but grow upon free surfaces are also innocent and well-organized; papilloma and mucous and fibrous polypi are examples.

These facts plainly establish the general truths that neoplasms

* Ericson : Science and Art of Surgery.

† Green : Pathology and Morbid Anatomy.

of inferior organization blend more or less with surrounding parts and that neoplasms of superior organization are usually shut off from them by limiting structures, or are situated upon surfaces and quite external.

Where the cells of embryonic growths obtain access to the interstices of adjoining connective tissue, they are sometimes arranged in alveolus-like spaces in this connective tissue. Scirrhus cancer and alveolar sarcoma exemplify such relations of embryonic tumours to the connective components of the tissues. There are also the relations of tumours to blood-vessels, lymphatics, and nerves. These may be glanced at in the next section.

§ 12. *Interpretation of these Relations.*

The association of capsulation with high organization and the absence of capsules in embryonic growths is a very striking fact, and yet the question of its significance seems not to have received the attention it deserves. We may be sure that the fact is not without meaning, and seeing how different are the clinical phenomena of embryonic and fully-developed neoplasms, the true explanation, if it can be divined, may be of service to us in other directions.

The capsulation of a tumour appears to be an indication of that resistance which tissues may be supposed to offer to the encroachments of tumours. It was postulated in § 5 that between the elements of a neoplasm and the elements of contiguous normal parts, there is a constant physiological antagonism. A tumour is an individual structure, and ever striving to spread at the expense of the organism while the organism is ever trying to keep it in check. One way in which the organism succeeds in setting limits to the advances of a tumour is by the erection of a defensive structure in the shape of a capsule. A capsule is not a product of the tumour-cells, but grows out from the encompassing tissues. To enucleate tumours and leave the capsules behind is a common procedure in surgery. Capsula-

tion, therefore, is an adaptation of the organism to resist the trespasses of a tumour, and it bears testimony to a partially successful resistance. With inconsiderable exceptions tumours that are bounded by connective tissue are benign—that is, beyond the mechanical inconveniences of their presence and their draught upon the nutritive material they are not specially hurtful. A well-circumscribed new growth is rarely fatal. On the other hand, diffuseness, from the absence of a capsule, is nearly co-extensive with malignancy. A tumour is said to be malignant when its elements penetrate into near and distant parts, and there reproduce the original growth. Malignancy is the consequence, not of mere increase of size, which may go on within capsules, but of metastasis. “It may be said generally, that the more the structure of a tumour is allied to a natural one the more localized and innocent it is, and the nearer it approaches to a simple cell-formation the more malignant it is in its nature, returning when removed, or infecting the system.”* Surgeons are accustomed to accept the existence of a capsule as a sign of innocence, though we shall learn in another chapter that innocence and malignancy depend on other conditions besides capsulation. It is, however, evident that capsules, mostly present in superior and benign growths, do denote some power of resistance in the organism; and that their absence in most inferior and malignant growths is an indication of weakness in the organism. But why is there this power of resistance where the growths are mature, and this weakness where they are immature? To answer adequately, there would be needed a survey of the known conditions of neoplasia, and for this special chapters are reserved. The reader must, therefore, take it upon trust, pending his examination of these chapters, that the answer is probably contained in a fact already referred to (p. 27), that fully-developed and benign tumours are due to a less deep-seated devitalization of tissue than obtains in undeveloped and malignant growths. We shall presently find that mature growths generally occur at an earlier period of life

* Wilks and Moxon : Op. cit.

than the immature. In fibroma and adenoma of the mamma "single women during their prime are most prone to be attacked;" whereas in cancer of this organ 81·20 % appear after the age of forty, and sarcomas "rarely attack the breasts of young women but rather those over thirty or thirty-five, and they are not uncommon in women about fifty years of age." A similar contrast is seen in the case of uterine myoma and uterine cancer, and in osteoma and sarcoma of the bones. It is true that sarcoma of the bones and some other parts is often met with in early life, but speaking generally it is undoubtedly a disease of mature and advanced life, as will shortly be shown, while all the benign tumours of the connective-tissue class are commonest in youth and middle age. Much evidence will be adduced to show also that there is usually a severity in the causes of malignant disease such as is rarely witnessed with innocent growths.

Observe, now, how remarkably these considerations illumine the facts. If innocent tumours are the products of centres set free by tissues whose reserve of vitality is relatively large—which the age and other conditions affirm—it accords with the established truths of organic development that the tumour-products of such tissues will exhibit high organization and the tissues themselves strength of resistance. Thus the superior development of innocent tumours, and the capsules which usually surround them, are correlative effects of one factor—relative power in the tissues; though this power is low enough for histogenic dissolution under the special circumstances which may have induced it in any given case. Conversely, the malignant tumours are the products of centres set free by tissues whose reserve of vitality is relatively small, and their inferior development and non-capsulation are correlative effects of this circumstance. It was expounded in § 5 that histogenic dissolution being the essential and only constant condition of neoplasia also supplies the condition of diminished tissue-resistance which exists in a greater or less degree in every instance of tumour-growth.

In those cases where tumours grow upon free surfaces—

some fibromas, warts, and polypi—the tissue-resistance is probably at a maximum; the neoplasms scarcely penetrate the substance of the body at all and sometimes they are completely severed from it by the natural efforts of the tissues.

It is needful to guard against an anthropocentric interpretation of the word “resistance.” I believe that the issue between a tumour and the tissues is of the simplest kind, nothing more than a competition for nutriment. It should not be understood that capsules and the growth of bone round tumours denote intentional and purposive resistance. In reality, as it seems to me, they are merely indications of reparative and nutritive vigour. As a tumour expands it presses upon adjacent parts and induces atrophy and disappearance of the cells in immediate contiguity. A capsule, filling the vacancy so caused, is an outgrowth in the directions of diminished resistance to growth precisely as is the growth of scar tissue, or the growth of connective tissue in chronic inflammation.* In the case of certain uncircumscribed benign tumours, as the diffuse lipoma, we may suppose the diffuseness to signify a limited power of independent growth such that the tumour fails to seriously interfere with the life of the tissues.

In concluding the last section it was said that the embryonic cells of cancers and alveolar sarcomas wandering from their places of birth find lodgment in the interstices of the connective tissue which forms what is called the stroma of the growth. The cells of glandular tumours often carve out for themselves definite spaces of alveolar form, and though generally they are grouped in these spaces without regularity occasionally the grouping is quite regular and the alveolus with its contained cells approaches closely to the structure of a normal acinus. In cylindrical epithelioma, or cancer of mucous glands, as of the rectum, there may be a formation of acini indistin-

* Cf. *Dissolution and Evolution and the Science of Medicine*, p. 121.

guishable from those of the healthy gut. "In these tumours the epithelial elements are similar to those of the mucous membrane from which they grow. They are cylindrical in shape, and are arranged perpendicularly to the walls of the alveoli in a manner precisely analogous to that of the columnar epithelium on the mucous surface."* These characters are due to the tendencies, here favoured and there checked by circumstances, of the new growth to reproduce the parent form.

The meshes in sarcoma are said to contain from one to four cells, but in cancer a larger number, and it is noteworthy that the cells of sarcoma are frequently attached to the walls of the alveolus while the cells of cancer are not.† In all probability this difference is connected with the unlikeness of relations to lymphatics and blood-vessels observed in sarcoma and cancer. The stroma of a cancer is supplied with blood-vessels, but they are not distributed to the cancer-cells. "They are limited to the stroma, and never pass into the epithelial masses." Correlatively, cancer is not disposed to affect the system by way of the blood-vessels, and the cancer cells lie free in the alveoli. Now, in sarcoma the blood-vessels are in direct contact with the cells of the new growth, and the walls of the young blood-vessels are often formed by them. Correlatively, sarcoma *is* disposed to affect the system by way of the blood-vessels, and the sarcoma cells are frequently attached to the walls of the alveoli. That the blood-vessels of the fibrous stroma enter directly into the groups of cells in sarcoma but not into those of cancer may be owing to the generic affinities of sarcoma cells and fibrous tissue.

The disposition shown by cancer to infect the system by way of the lymphatics has been explained by the free communication of the alveoli with the lymphatic vessels.

In the relations of the tumour-cells to the connective tissue

* Green: Op. cit. p. 188.

† Hamilton: A Text-book of Pathology.

we often see again, especially in scirrhus cancer, evidence of a survival of the tissues in their contest with the neoplasm. The cells in the alveoli may wither and perish so completely that only connective tissue is left. The vacant spaces become filled up by an outgrowth of the stroma, and this by contraction and consolidation confers extreme hardness upon the neoplasm.

Finally, it must be noted that tumours are destitute of nerves. This fact surely agrees very remarkably with our assumption that neoplasia exemplifies a reversion to primitive modes of life. Resulting from a process of true genesis tumours are distinct individuals and functionally uncompounded with the parent; hence they are not included in the function-compounding system—the nervous system—nor do they any more than unicellular organisms require for their existence a functional consensus of their own elements. The development in tumours of integrating structures or nerves is precluded by the nature of neoplasia as here conceived. We have said that a tumour is not an accrescence or continuous growth, but a discontinuous growth in which pre-existing attachments to the parent tissues are dissolved. Such attachments as remain or become organized, proceed from the power of the tumour-elements to draw food-material along the already formed channels, which may undergo extensions as new blood-vessels. From the cells of the most compact fibroma or adenoma to the quite discrete cells of sarcomas and cancers we perceive unimpaired the simple functions of nutriment-absorption and procreation, and it is the retention of these primordial endowments that serves to give to tumours the only union between them and the organism we are able to discover—that conferred by their inclusion in the nutriment-distributing system. Some writers have declared that the cardinal characteristic of tumours, their self-dependence, is consequent on the absence of nerves in them. I take the truth to be that they have no nerves because they are self-dependent.

§ 13. *The Modes of Tumour-growth.*

We have considered in what way tumours are probably born (§ 4 and § 7), and now we have to consider in what way they grow. A tumour may augment in bulk by interstitial increase, by surface increase, or by infiltration. Benign tumours generally add to their substance by interstitial or central growth. When the initial units, say of a myoma, have been liberated as we suppose by the generative dissolution of a group of normal tissue-cells, the germs throughout the aggregate divide and acquire more complex structure as in ordinary growth and development.

In surface increase, occurring in both benign and malignant tumours, the multiplication of cells takes place at the periphery. Here are the youngest portions of the tumour, and often it is found that while growth is going on at the surface, the central portions are dead or degenerating.

Growth by infiltration is also growth from the periphery, but infiltration is a property of the embryonic cancers and sarcomas though not absolutely confined to them. The cells of these neoplasms form, for the most part, exceedingly loose aggregations. The self-dependence which we have seen to be so characteristic of tumour-masses is, in the embryonic tumours, extended to the individual units. The cells of a sarcoma or carcinoma may be regarded as separate and distinct entities; they sever themselves from the primary aggregate, and each has the capacity for drawing nourishment by simple absorption from the albuminous fluids and solids everywhere contained in the tissues. We have just now noted that, like normal structures, the mass of a tumour is fed by vessels, but with the discrete cells of embryonic growths there is not even dependence upon organized channels of nutritive supply; either singly or in groups, the emigrant cells upon the confines of a cancer or sarcoma shoot out into the tissues in all directions, and as they absorb sustenance from the substance of the parts

they penetrate, they increase in number by the usual processes of cell-multiplication. This is growth by infiltration.

In general, the mass of a tumour is developed from a single centre; but the same part or organ may exhibit many centres. Sometimes the removal of a mammary adenoma will disclose the existence of other minute and quite independent growths,* and in the uterus it is common to see several myomas; indeed, the uterus has been found wholly converted into multiple tumours. Cancer has been known to start from more than one distinct and independent focus, as in the breast and uterus. Dr. J. Williams thus refers to a case reported in his work on Cancer of the Uterus. "Here we have cancer developing from two points of origin, if not from three—that is, from the glands just below the inner orifice, from glands near the external orifice, and from the squamous surface of the portio-vaginalis."

Already it has been mentioned (p. 27) that the histogenic dissolution from which each benign tumour is supposed to originate, is probably confined to a very limited area of tissue, and doubtless this is usually the case in cancer and sarcoma, but there are grounds for thinking that either simultaneously or in rapid succession extensive tracts of tissue germinate in some cases of cancer. The wonderfully quick growth, and the histological appearances point strongly to this possibility. As the elements of sarcoma or cancer invade the adjacent parts the neoplastic structure is gradually substituted for the normal structure. A good illustration, among numberless others, is supplied by the specimen No. 529 in the Hunterian Museum. This preparation is a longitudinal half section of a femur involved by a "brain-like tumour," probably a sarcoma. The new growth has supplanted by its own substance every visible trace of osseous tissue from the middle and lower part of the bone. A similar change is effected by cancer, and though some structures, as cartilage and arteries, are more refractory than others to these influences of infiltrating growths, all the tissues

* Bryant: Diseases of the Breast, p. 101.

of a part may be alike replaced by the neoplasm. "Thus the scirrhus cancer of the breast, though limited for a time to the mammary gland, at length extends beyond it, and gradually occupies every surrounding part alike; thus, the epithelial cancer extends from the integument of the lip to its muscles, glands, and all deeper tissues, and thence to the gum and jaw; and thus the medullary cancer grows into and through the walls of blood-vessels and other canals, and extends among their contents along their cavities."*

Let us now look at the facts here grouped when they are mirrored by our hypothesis. To explain the modes of growth observed in tumours, it is required mainly to repeat the argument used to interpret the relations of tumours to surrounding parts (§ 12). It has been set forth (§ 4) that the elements of tumours are direct descendants of the tissues, and that having originated from them by histogenic dissolution, they tend to rehearse the parental life. It agrees, then, that they tend to grow as the natural tissues grow, though, of course, as isolable masses. Now, if we provisionally grant that "fully-developed and benign tumours are due to a less deep-seated devitalization of tissue than obtains in undeveloped and malignant growths" (p. 27), it further agrees that their mode of growth is as compact aggregates, and that the mode of growth in undeveloped tumours is as diffuse aggregates. Structural integration is, perhaps, everywhere one of the concomitants of structural complexity, and both are dependant, in organisms or tissues, on the energy stored up in the molecular constitution. The autonomy shown by the individual units of cancers and sarcomas, their growth by infiltration, is related therefore to their inherent feebleness, consequent on feebleness in the mother tissues. But, as we have seen, this very weakness in development goes with strength in another direction. What they lack in the energies which run to integration and differentiation is offset by the

* Paget; Lectures on Surgical Pathology, p. 814.

simplicity of their processes of nutrition and their immense fecundity. Being able, as we have seen, to extract nutriment indifferently from muscle, gland, bone, and other tissues, and the energy so acquired having no outlet in development, the only remaining outlet, while life continues, is in multiplication.

So that we are not at a loss to explain, consistently with our hypothesis, the modes of growth in tumours. It remains, however, to determine, more exactly if possible, the process or processes by which infiltrating tumours induce those changes in normal parts which have just been referred to. Does a sarcoma or cancer remove the substance of bone, muscle, or gland, simply by consuming it and then occupying its place? or do the elements of normal tissues become metamorphosed by contact with the elements of the new growth? It is probable that the changes in question are produced by both of these processes. The microscopic appearances suggested to Dr. Creighton that the normal tissues might possibly be changed into the substance of a neoplasm by some influence of embryonic tumour-cells analogous to that of sperm upon germ. Speaking of cancerous infection of the mammary gland, Dr. Creighton says: "Whatever the infective influence may have been, it touches all the quiescent cells over a certain area simultaneously; a 'territory' of tissue, larger or smaller as the case may be, but always involving a number of cells, assumes the embryonic life throughout its whole extent, and goes through all the steps of the transformation towards the epithelial type and grouping, as if its cells had received one common impact."* And appearances like these have been recorded by others, but without Dr. Creighton's hypothesis of spermatogenic influence as the interpretation. Dr. Coats thus refers to a case where the humerus was replaced by a soft sarcoma: "It is only at the extremities that any of the bone remains, and here the appearance is not as if the bone were being destroyed by a myelogenous tumour, but as if it were actually expanding into the tumour."† But definite observations have been made

* Physiology and Pathology of the Breast, p. 381.

† Manual of Pathology, p. 751.

which demonstrate, perhaps conclusively, that the tissues of a part are metamorphosed into embryonic cells. The reader's attention is called to the adjoined figures (Fig. 5), which are reproduced from Sir James Paget's "Surgical Pathology," page 805. They are intended to illustrate changes in muscular fibre witnessed by Professor Turner, in a case of infiltrating tumour of the scapula and its muscles. It will best suit my purpose to quote the text accompanying the figures in Sir James Paget's work: "At *a* in Figure 131, a muscular fibre is shown, in which multiplication of the nuclei of the muscle-corpuscles has taken place, and the new-formed structures are arranged either in linear series or in little masses within the



Fig. 5.

sarcolemma. At *b*, the multiplication is much further advanced, the proper sarcous substance has entirely disappeared, and the sarcolemma is filled with a young brood of corpuscles. In other localities a more advanced stage was observed. The fibres were jagged and broken, and the corpuscles developed in their interior, being set free, formed collections of small new cells within the substance of the muscle. By the extension of this process in different parts of the muscle, the fibres were in a great measure disintegrated—the increase in the size of the cancer being obviously due to the multiplication of the corpuscles within the muscular fibre and to their subsequent liberation." Without stopping to adduce further facts of this

order, let us at once inquire concerning the nature of these changes whereby, as Sir James Paget remarks, the tumour increases its substance. I think we may, without any misgivings, set aside the hypothesis of spermatic influence; there is apparently no immediate evidence to support it, and it is quite overborne by indirect considerations. *This metamorphosis of muscle is histogenic dissolution; the muscular tissue, as such, has obviously been annihilated in the production of offspring.* The process by which, as we have assumed, all tumours take origin, is here seen to be the means by which embryonic tumours spread, and it is easy to understand how this happens our hypothesis being true. The condition-precedent of histogenic dissolution is the depletion of the vital reserve, and it has been stated that in the tissues of a part where an embryonic tumour starts this reserve is very low. Now as the cells of an infiltrating growth insert themselves into the substance of the tissues, and by their prepotent powers of absorption and multiplication rob these tissues of nutriment, and perhaps consume the very protoplasm of the tissue-cells, the individual life is brought to a close from starvation, and the tissues dissolve into embryos. (Compare Fig. 5 with Figs. 1, 2, 3, and 4.)

This then is probably the nature of the contact-action of lowly-organized tumours. It results, therefore, that we must add to the recognized forms of growth in tumours growth by histogenic dissolution.

It is worth mentioning that these considerations furnish an adequate reason for the frequent presence in cancerous substance of multitudes of nuclei and the detritus of tissue.

§ 14. *Summary of the Morphology of Tumours.*

That there should be an almost invariable coincidence between the enunciated hypothesis and facts so varied as those comprised in the morphology of tumours, must be held of good augury for its ultimate confirmation. Seemingly there are no serious discrepancies. We have found that positive

evidence is not wanting of that upon which the hypothesis really hinges; the fact of histogenic dissolution. Under certain auspices the genesis of tumours by this process is actually observable; or at least the immediate results are observable and are such as clearly to identify the two. Then the morphological characters of the undeveloped elements of tumours quite fulfil anticipations. In their primordial sphericity and simplicity of parts, in their modes of aggregation, reproduction, and growth, we see a more or less complete congruity with the supposition that neoplasia is a reversion to the genesis of unicellular organisms.

The histology of tumours and their contiguity to the tissues they bear a likeness showed us unmistakably that the tissues at large are the parents of tumours. By considering that neoplasms begin as embryo-cells born of the different tissues, it was found possible to comprehend both the morphology of any isolated group of tumour-elements, and also the numberless gradations of form and feature seen in individual tumours and in tumours arranged in natural classes.

In dealing with the modes of growth in tumours and the relations of tumours to surrounding parts, the interpretations required us to submit an induction that rests on facts interspersed through succeeding chapters, but by its provisional acceptance some exceedingly abstruse matters were illuminated and seen to be in harmony with the hypothesis.

Having thus passed under inspection the truths connected with the forms of tumours, we may now proceed to contemplate the factors.

CHAPTER III.

THE GENERAL CONDITIONS OF TUMOUR-DISEASE.

The relative Frequency of Tumours of the Different Tissues.—The relative Frequency of Tumours in the Different Organs.—The influence of General Nutrition upon the Genesis of Tumours.—The influence of Age upon the Genesis of Tumours.—The Growth of Tumours as related to Nutrition.—Summary of the General Conditions of Tumour-disease.

§ 15. *The Relative Frequency of Tumours of the Different Tissues.*

We have reviewed the most important facts connected with the morphology of tumours, and have considered how they stand in relation to the hypothesis advanced. It is required now that we should deal in like manner with the accumulated observations upon the *circumstances* attending the birth and life of new growths. The data yielded by such observations fall into two major divisions; there are the conditions, of a more or less general character occurring both within and without the organism and known as the accompaniments of neoplasia; and there are the conditions of a more or less special character, for the most part externally incident. The first of these divisions, the general conditions of neoplasia, forms the matter of the present chapter.

But little notice has been taken of the fact that the various tissues of the body are reproduced in tumours with unequal frequency. If this fact were expressed in the terms of our hypothesis, we should say that the different tissues are liable in different degrees to form tumours. It is observed that growths of fibrous tissue—embryonic and mature—of fatty tissue, and epithelial tissue, are exceedingly common as

compared with growths of muscle, nerve fibre, or ganglionic nerve tissue. Striated myomata "are exceedingly rare, only two or three examples having been recorded, and these were congenital." "True neuroma is rarely met with, and is among the least frequent of all the new formations."* Speaking broadly, the most specialized tissues are less often represented in tumours than the least specialized. Of 11,100 new growths of all kinds, nearly 7000 were of unspecialized varieties.† What, probably, is the significance of this? Doubtless it is an instance of that inverse relation between reproduction and specialization seen throughout the whole organic kingdom. It has been established as one of the laws of reproduction that whatever energy is used up for increase of mass, for increase of structure, and for functional work, is so much deducted from the energy that might be available for productive processes.‡ So that the relative scarcity of myoma and neuroma is in consonance with the fact that reproductive power tends to diminish as specialization or structural complexity increases. The indications of this law both in the animal and vegetable worlds are unmistakable, nevertheless the evidence of it is almost inextricably entangled by qualifying circumstances. And it is similarly entangled as the generalization applies to neoplasia. For, taking the organism as a whole, we see in the case of myoma that this is an uncommon tumour, whether of striated or non-striated muscle, yet it is far from being so in the uterus. Here we may be confident the exception is due to exceptional circumstances. But it is not worth while to thresh out the matter with thoroughness. There is no doubt about the general fact, the higher tissues are decidedly less prone to form tumours than the lower; and in the relatively rapid growth of the unspecialized cancers and sarcomata, and in the small size of pure myomas and neuromas, neoplasia affords other clear illustrations of the law. We must be content with the probable truth of this explanation

* Green : Op. cit.

† Roger Williams : *The Influence of Sex in Disease*, p. 12.

‡ Spencer : *Principles of Biology*, vol. ii. chap. vii.

of the datum in question, and note its agreement with the conception of neoplasia as a form of genesis or true reproduction.

§ 16. *The Relative Frequency of Tumours* in the Different Organs.*

From the relative frequency of tumours personating or arising from the several sorts of tissue, we pass naturally to the relative liability of the organs to new growths. The most striking contrasts are met with. On one hand, primary tumours of the heart are scarcely known, and on the other, myomas of the uterus are so common that one woman in every ten is said to be afflicted; and sometimes the centres of development are so numerous that "there may be as many as fifty attached to the same uterus."* In my previous volume, I have submitted the induction that some relationship apparently exists between the frequency of tumours in different organs and the distribution of these organs upon the vascular tree. With a few exceptions the further we proceed from the central organ (the heart) of the nutriment-distributing system, the more prone the organs and viscera appear to be to the formation of tumours. Before we venture to interpret, let us look well at the facts.

Of tumours growing primarily and independently from either the pericardium or the substance of the heart, there are scarcely any indubitable examples. Dr. Wilks and Dr. Moxon are able out of their vast experience to point to only two specimens, and these are of polypoid tumours growing from the left auricle. Cancer of the heart is probably always either an extension of cancer in neighbouring parts, as of the mediastinum; or it is secondary to cancer of remote organs. Ziegler says: "Of the true tumours several kinds may attack the heart primarily, such as sarcoma, fibroma, lipoma, myxoma, and myoma, but they are all of them rare." We also read that "Primary tumours of the heart are exceedingly rare; but a primary sarcoma of the endocardium has been described as also primary fibroma, myoma, and lipoma" (*Coats*). Allowing for errors of observation through

* *Coats*: Manual of Pathology, p. 685.

which secondary tumours may have been mistaken for primary ones, it is clear that the cardiac substance enjoys a singularly slight liability to tumour-disease.

The lungs are nearly as often as the heart exempt from primary tumours. "Primary tumours of the lung or bronchi are rare" (*Ziegler*). Cases of fibroma in the form of nodules round the bronchi and of enchondromata, starting from the bronchial cartilages, have been described. Of cancer of the pulmonary (not bronchial) tissue, there are scarcely any well-authenticated instances. "A *true primary* cancer of the lung is so rare that we have only one specimen to show."*

In the liver, tumours are seen oftener than in the lung; but omitting cavernous angioma, primary growths are comparatively seldom found in the hepatic substance. "It is rarely the seat of innocent or non-infectious tumours, and only two or three examples of cancer have been met with where the liver was the only organ affected."† The liver, however, is most frequently the seat of secondary growths.

And tumours of the spleen are very infrequently observed; "primary cancer of the spleen is exceedingly rare."‡ But when we pass to the pancreas and kidney, tumour-disease becomes less infrequent though not very notably so. Nodular fibromata are said to occur frequently in the kidney, and small adenomata have been described.§ Both in the kidney and pancreas cancer has been observed many times.

Receding in the same direction still further from the centre of the vascular system, we reach the bladder, in which the polypoid fibroma is somewhat common. Primary carcinoma is met with, though rarely.

Of the organs of generation in the male the testicles are, perhaps, peculiarly disposed to generate morbid growths. Sarcomas and cancers are the usual forms, and less commonly enchondroma, fibroma, myoma, &c. It is worth noting that the

* Wilks and Moxon: *Pathological Anatomy*.

† *Ibid.*

‡ Wilks and Moxon: *Op. cit.*

§ *Ziegler: Op. cit.*

testicles are nourished by the long and slender spermatic arteries, which arise from the abdominal aorta as high as the point of origin of the renal arteries. In the penis the usual form of new growth is cancer of the *glans penis*.

Of the organs of generation in the female, the ovaries, analogous to the testes, though better circumstanced in respect of their blood-supply, are very ready to undergo neoplastic degeneration.

If we pass upwards from the heart and leave for the present the entire alimentary tract, we may recall the rarity of tumours of the lungs which organs are in immediate relation with the heart. Now the bronchus and trachea enjoy a similar though not equal immunity, for cancer of the bronchi has been several times described, but the distantly-situated larynx gives origin to many kinds of new growth. These include papilloma, fibroma, mucous polypi, sarcoma, and epithelioma. The favourite seats, too, are the projecting vocal cords and their neighbourhood.

This general proneness to tumour-disease displayed by tissues according as they are near to or far removed from the trunk of the arterial tree, appears in another way. We may roughly regard the arteries of the entire organism, and of its organic or visceral parts, as having central and peripheral dispositions. Thus, for the whole body there are the great central arterial trunks; the general external periphery, the skin; and the general internal (involved) periphery, the lining tissues of the alimentary canal. For the separate organs there are usually a fundus, body, or base—as of the uterus, stomach, and mamma—and extremities and surfaces. Now these terminal parts, whether surfaces or points, are generally at the *ends of the vascular branches*; and it is remarkable that here neoplasms are disposed to take origin.

In the case of the first of these divisions, how much greater is the proclivity of the skin and alimentary canal to generate tumours than the interperipheric tissues. As cutaneous growths we meet with cancer, keloid, warts, fibroma moluscum, lipoma, sarcoma, &c. In the alimentary canal the gastric and duodenal

tissues furnish a very large number of cancers. And their usual starting-points are the pyloric and œsophageal orifices. Cancers of the stomach do not often grow from the fundus, nor other tumours from the peritoneal surfaces where the stems of the vessels are. Apparently a similar relation to the vascular supply as this supply is dependent on distance from the heart, is traceable with tumours of the intestine. In the cæcum, sigmoid flexure, and rectum, cancers are observed with a gradually increasing frequency as the terminus of the gut is approached. But in the centrally-situated ileum and jejunum they are scarcely ever found. "So rare is cancer of the ileum that its ever occurring in this portion of the bowel (unless through the contamination of adjacent disease) has been made matter of question."*

And if we examine the case of the uterus, or of the mammary gland, similar facts are pressed upon us. It is chiefly at the peripheries of the visceral systems of vessels, at the orifices and near the internal surface of the uterus, and near the external surface and the nipple of the mamma, that neoplasms first appear. Note also the common situations of tumours of the mouth, nose, and penis. From the lips and edges of the tongue epithelioma springs; or it starts from the alæ of the nose. Epithelioma of the penis begins in the *glans penis* or the prepuce.

In the bones, osteo-sarcoma is disposed to arise at the extremities of long bones, and from the external and internal peripheries, the medulla and periosteum. Very striking is the fact that sarcoma has a predilection for those parts of the bones where growth ceases last, *i.e.*, at the ends opposite to the line of direction of the nutrient arteries. The lower epiphysis of the femur is the last to join the shaft, and the nutrient arteries are oppositely directed-towards the upper epiphysis. Of seventeen central tumours of the femur, ten were situated at the lower epiphysis. The upper epiphysis of the tibia and humerus join the shafts at twenty-five and twenty years respectively,

* Walshe: The Nature and Treatment of Cancer.

when growth in the rest of the bone is complete; and the nutrient arteries are directed downwards in both bones. Of thirteen tumours of the tibia, "eleven started in the upper epiphysis; and of eight affecting the humerus, all but one were in the upper epiphysis."* And the benign tumours of bone are not very dissimilarly distributed. Osteoma affects mostly the ends of the long bones, and the fingers and toes are attacked by enchondroma much more frequently than other parts. Upon the ends of divided nerves there may occur small fibro-neuromata.

Can the validity of this induction be questioned? That some such relation to vascular distribution does exist seems irresistible. I have elsewhere argued that the genesis of tumours may be furthered by relative innutrition, and that owing to the increased obstruction to the propulsion of blood with each increment of distance from the heart, distant parts will, if other things are equal, be less favourably situated for obtaining nourishment than will the heart and organs clustered round the great arterial bunks. But of course other things are not always equal. An organ far from the heart may be so much more richly provided with blood-vessels than one near to it that the disadvantage of distance may possibly be compensated. I say *possibly* compensated, for it is evident on reflection that high vascularity in a normal tissue does not denote *excess* of blood. The nutritive matter distributed is strictly proportionate to physiological needs. If there is much blood in any part, much is used up in function. We cannot, therefore, allow a great deal for this qualification, and the evidence is too strong to be gainsaid that, other things equal, remoteness from the centre of blood-circulation is unfavourable to the acquirement of nutritive material. As *a posteriori* evidence it is sufficient to mention gangrene of the extremities in old people, the feebleness of repair in ulcers of the lower limbs, and the sensitiveness of the very vascular brain to

* Butlin: Sarcoma and Carcinoma.

deficiency of food or diminution of cardiac power. Still, even if it be true that relative innutrition in some degree furthers neoplasia, there *are* qualifications of much account. The life-conditions of the various organs are extremely unlike, apart from the differences of distribution upon the branches of the arterial system. The common seats of tumours, the skin, the alimentary canal, the organs of the sexual system, and the osseous system, have the most varied converse with the energies of the outer world, and these circumstances as determinants of tumour-disease may quite outweigh the circumstance of blood-supply. We shall very shortly see, I think, that they do. Evidence will be presented from which the conclusion is inevitable that for practical purposes the greater number of tumours are caused by locally-incident forces. Nevertheless, I think that some influence in the genesis of tumours must be granted to the factor we are considering, and so thinking it is requisite to inquire in what way the influence is probably exerted.

Tumour-genesis has been ascribed (§ 4) to the casting off of new centres of development in tissue-cells, whose vital changes are beginning to fail. One of the ways in which a cessation of vital changes may be accelerated, either in the organism or in any of its parts, is by deficiency of nutriment, and we may very well believe that wherever in the body this condition conspires with other conditions, there the tendency to tumour-disease will be most distinct. In studying the modes of growth in tumours, we met with an instance of the operation of innutrition in promoting histogenic dissolution (p. 52). What is here supposed in the case of tumours receives considerable support from parallel phenomena observed in plants. By the hypothesis tumour-formation is a process of discontinuous growth or true genesis. Fruit-bearing in trees is also discontinuous growth, as leaf-bearing is continuous, and it is certain that the discontinuous process is favoured in these organisms by relative innutrition. Referring to this fact, Mr. Spencer observes * :—"The rela-

* Principles of Biology, vol. i. chap. vii.

tion between fructification and innutrition among plants was long ago asserted by a German biologist—by Wolff, I am told. When some years ago I met with the assertion I was not acquainted with the evidence on which it rested. Since that time, however, I have, when occasion favoured, examined into the facts for myself. The result has been a conviction, strengthened by every further inquiry, that such a relation exists. Uniaxial plants begin to produce their lateral flowering axes only after the main axis has developed the great mass of its leaves and is showing its diminished nutrition by smaller leaves or stunted internodes. In multiaxial plants two, three, or more generations of leaf-bearing axes or sexless individuals are produced before any seed-bearing individuals show themselves. When, after the first stage of rapid growth and agamogenetic multiplication, some gamogenetic individuals arise, they do so where the nutrition is least; not on the main axis or on the secondary axes, but on the axes that are most removed from the channels which supply nutriment. Again, a flowering axis is commonly less bulky than the others; either much shorter, or, if long, much thinner. And further, it is an axis of which the terminal internodes are undeveloped. The foliar organs, which instead of becoming leaves become sepals and petals and stamens, follow each other in close succession, instead of being separated by portions of still-growing axis. Another group of evidences meets us when we observe the variations of fruit-bearing that accompany any variations of nutrition in the plant regarded as a whole. Besides finding, as above, that gamogenesis commences only when the luxuriance of early growth has been somewhat checked by the extension of the remote parts of the plant to some distance from the roots, we find that gamogenesis is induced at an earlier stage than usual by checking the nutrition. Trees are made to fruit while still quite small by cutting their roots or by putting them in pots; and luxuriant branches which have had the flow of sap into them diminished by what gardeners call “ringing,” begin to produce flower-shoots instead of leaf-shoots. Moreover, it is to be remarked that

trees which, by flowering early in the year, seem to show a direct relation between gamogenesis and increasing nutrition, really do the reverse; for in such trees the flowering buds are formed in the autumn—that structure which determines these buds into sexual individuals is given when the nutrition is declining. Conversely, very high nutrition in plants prevents or arrests gamogenesis.” Of the cryptogamia, too, we read that “fissiparously-multiplying cells in some cases fly asunder, while in other cases they unite into threads or laminæ or masses; and fronds originating proliferously from other fronds, sometimes when mature disconnect themselves from their parents and sometimes continue attached to them. Whether they do or do not part is clearly determined by their nutrition . . . That disunion is really a consequence of relative innutrition, is clear *a posteriori*. On the one hand, the separation of the new individuals, whether in germs or as developed aggregates, is a decaying away of the connecting tissue; and this implies that the connecting tissue has ceased to perform its function as a channel of nutriment.” And this consideration is just as applicable to the parts of single cells as it is to an assemblage of cells. It may be seen in the cultivation of bacilli how the organisms grow to gigantic proportions and multiply by fission in a rich soil, whereas with a scant supply of nutriment they are smaller and multiply by spore-formation. In cultures of bacilli it is found that when the gelatine or other culture-medium is becoming exhausted the bacilli are resolved into spores. With test-tube cultures, spore-formation takes place from above downwards as the food is used up: on the surface of the gelatine where the nutriment has been consumed spores are abundant, but in the deeper parts multiplication is proceeding by simple division of the bacillary rods.

I do not doubt that innutrition, arising from the relative distances of parts from the centre of blood-supply, is a sensible though not practically important factor in some cases of neoplasia, but at this stage we cannot form a just estimate of its efficiency. We must wait until we come to estimate the efficiency of other factors.

§ 17. *The Influence of General Nutrition upon the Genesis of Tumours.*

The contents of the preceding section suggest the question whether the general food-supply has any connection with the genesis of tumours? What is the influence of general innutrition from deficiency of food or of general high nutrition from excess of food? On these points the information contained in the reports of cases possesses little clear signification, and it will be more convenient to deal with the facts as we encounter them in the special divisions of our subject. Meanwhile, it may be said that the influence of food-supply, like the influence of innutrition due to locality, appears to be subordinate. The *growth* of tumours (§ 19) is beyond all doubt promoted by high nutrition, and there is *a priori* warrant for thinking that excess of food will, when other conditions are favourable, assist in the *genesis* of tumours. That it should do so does not negative what has just been said as to the favourableness of innutrition. When the tissues are ripe for histogenic dissolution, when the protoplasm of the cells is no longer capable of undergoing the chemical and physical changes needful for individual life, a superabundance of food will not retard the end of that life and the formation of new centres, just as a superabundance of food will not retard the end of a man who is dying from old age. There is reason to believe that the tissues being ready for histogenic dissolution high nutrition may facilitate the process. In the case of plants, fructification takes place at those terminal points where nutritive changes are least active; but unless the general nutrition reaches a certain level reproduction will not set in at all. When once inaugurated, it will, too, be furthered by abundant nourishment. "Were it otherwise, the manuring of fields that are to bear seed-crops would be not simply useless but injurious. Were it otherwise, dunging the roots of a fruit-tree would in all cases be impolitic; instead of being impolitic only when the growth of sexless axes is still luxuriant. Were it otherwise, a tree which has borne a heavy crop should,

by the consequent depletion, be led to bear a still heavier crop next year; whereas it is apt to be wholly or partially barren next year—has to recover a state of tolerably high nutrition before its sexual genesis again becomes large.” Among animals also this is evident; a good supply of nourishment facilitates reproduction, and the casting off of new individuals is generally the casting off of a surplus—of something over and above what is required for individuation.

I think we shall find the special facts as to the conditions of tumour-disease in harmony with this reasoning. It will not transpire as we examine cases that a state of high nutrition is among the real causes of tumours, but that the data countenance a belief in the favourableness of high nutrition when this is accessory to the actual and effective factors.

With respect to the influence of low nutrition from insufficient food, cases seem to show that occasionally this is a true co-operative cause.

§ 18. *The Influence of Age upon the Genesis of Tumours.*

In the chapter to succeed the present one the special conditions of tumour-disease, as it occurs in particular organs and parts, will be dealt with. Then it will be necessary to consider the influence of age in each class of cases. But the present survey of the general conditions of tumour-disease would be incomplete without some brief references to this branch of our subject.

Though the various sorts of tumour differ as to the period of life at which they usually occur, yet a certain degree of age is distinctly favourable for all. “Tumours of every kind are far more common during or after the middle period of life.”* Myo-fibroma of the uterus is not met with before puberty, and the age of greatest liability is from thirty to thirty-five years. Adenoma of the mamma is observed between puberty and the age of fifty years. Of sixty-three cases of central tumours of bone, only two occurred before the age of sixteen. Of fifty-six cases of sub-periosteal tumours, four-fifths occurred between the ages of sixteen and forty.

* Holmes and Hulke: System of Surgery.

But the favourableness of years is still more pronounced in cancer. Almost exclusively this is a disease of middle and late life. Walshe has shown that the number of deaths from cancer in proportion to the population increases with each decade until the eightieth year.* From the following table of cases collected by Sir James Paget we may compute the rate of increase as age advances to the fiftieth year. In 772 cases of cancer of all kinds the ages were as follows:—

Under 10 years 27			
Between 10 and 20	„	30	
„ 20 „ 30	„	78	
„ 30 „ 40	„	130	
„ 40 „ 50	„	200	
„ 50 „ 60	„	152	
„ 60 „ 70	„	98	
„ 70 „ 80	„	57	

Observations upon this disease made with the greater accuracy of modern methods would lead us to think that many of the cases above in persons under thirty years of age were not cases of cancer. At the present time, cancer before the twenty-first year is most rarely seen. “The malignant glioma of the eyeball and sarcomatous tumours of the testicle and bone, being formerly classed as encephaloid cancer, that disease was said not to be uncommon in children. Now that these are excluded, all forms of cancer may be said to be almost unknown under twenty.”† Yet there have been undoubted instances in early youth. Allingham has seen encephaloid of the rectum rapidly fatal in a boy of seventeen, and mentions a case of scirrhus in a boy of thirteen. A case of soot-cancer is recorded in a child of eight and a half.‡ And others might be referred to, but these exceptions leave undisturbed the general truth that cancer is a disease of middle and late life.

Sarcoma is by no means unknown in childhood and youth,

* The Nature and Treatment of Cancer.

† Eriksen : Science and Art of Surgery, 9th ed.

‡ Crocker : Diseases of the Skin.

but like cancer, it is much oftener seen late in life. Sarcoma of the skin seldom appears before maturity. Sarcoma of the breast attacks "those over thirty or thirty-five, and is not uncommon in women about fifty years of age."* Dr. Hamilton says that some of the most typical sarcomata he has met with were taken from persons over sixty years of age.† "The subjects of the spindle-celled sarcomas were from ten months to forty-five years old, but nearly all the cases occurred in persons under ten years old or between twenty-five and forty years."‡ The age-relations of round-celled sarcoma of the testis are nearly the same (*Butlin*).

Deferring for the present the notice of further facts connected with the age-conditions of tumour-disease, we may consider the general truths which the foregoing data disclose. It is certain that neoplasia at large has for one of its conditions a certain degree of tissue maturity; that cancer, almost without exception, is a disease of mature and advanced life; and that early youth and adult age are favourable to sarcoma. Can these inductions be assimilated with our hypothesis? I think it enables us to understand them as does no other hypothesis. If neoplasia is primarily and essentially due to histogenic dissolution from the impending cessation of local tissue-life (§ 4), then maturity and senility must needs be propitious. The longer the life of the organism the greater the number of stimuli which its tissues have been called upon to respond to, and therefore the smaller the remaining store of tissue-vitality. That as age increases vitality decreases is shown by the gradual enfeeblement of digestion and assimilation, by the slowing rhythms of the functions, by less and less ability to withstand the forces of the environment. The daily and hourly resistances to be met by the organism in the performance of its functions, are the means by which the vitality of its units is consumed. Age, therefore, affords beyond other circumstances a preparation for changes which depend on exhaustion of the energies

* Bryant: Diseases of the Breast.

† A Text-Book of Pathology.

‡ Butlin: Sarcoma and Carcinoma.

cognized as vital. As a predisposing cause, it supplies in the presence of other conditions the state of tissue-life supposed to be needful for histogenic dissolution, and it supplies at the same time a diminished resistance to the growth of the liberated germs. It is as a predisposing factor that age appears in the conditions of the cases that will presently come before us, but sometimes it will be seen to be the only assignable cause, and the present argument will prepare us to admit its occasional sufficiency.

The ages of the subjects of sarcoma show that, next to maturity and senility, infancy and childhood are the most favourable periods of life. It appears likely, for definite truth can be reached only by the careful study of individual cases, that the tenderness and weakness of childhood play the same part in the genesis of sarcoma that we have supposed is played by the lessened rigour of advanced life.

§ 19. *The Growth of Tumours as related to Nutrition.*

There are many facts which show that the growth of tumours, like the growth of other organic aggregates, is active or inactive as the nutritive processes are active or inactive. This is shown in a variety of ways, and often by growth *towards* the source of nutritive supply. In epithelioma of the skin there may be seen columnar clusters of tumour-cells extending from the surface-layers of the skin and dipping deeply into the underlying cutis. Here, probably, the downward extension of these cells is determined in part by the vascularity of the structures penetrated, and in part by the resisting power of the tissues. In what is known as flat epithelioma, the above-mentioned being the infiltrating form, the tumour-cells tend to increase laterally. Here, evidently, the conditions are not quite identical. Perhaps the vital resistance of the lower strata of cutaneous cells neutralizes the influence of vascularity. "In the superficial form the advancing epithelium is for a long time unable to penetrate the strong firm bundles of the corium, and, as Erasmus

Wilson has expressed it, contents itself with cropping off the highly organized *corpus papillare*.”* There is also a warty form of epithelioma where the cancerous structure sprouts upon the surface of the skin, possibly because in this variety still greater resistance is offered by the subcutaneous tissues. It is necessary to speak with diffidence of the causes of these peculiarities, for we do not yet know all the circumstances of their occurrence. We saw (§§ 11 and 12) from a survey of the whole series of neoplastic formations, that, broadly speaking, the degree of tissue-resistance is inversely measured by the extent to which a growth incorporates itself with the substance of the body. The benign and less malignant tumours are generally prevented from seriously assailing the integrity of the organism by being extended upon surfaces or enclosed in capsules.

Cancer of the mucous membranes, as of the mouth or uterus, shows equally well the advance of the neoplasm in the direction of blood-supply. Sometimes, in cancer of the stomach, the mucous membrane is not greatly altered. “The mucous membrane exhibits a notable power of resistance to the encroachment of the disease. Even the stratum lying immediately over cancerous substance is slow to undergo infiltration or to ulcerate; its prevailing tendency is to become hypertrophous.”†

The coarse anatomy of cancer yields similar testimony. When this disease affects the stomach, it rarely extends into the duodenum, but generally into the gastric tissues, where the soil is certainly more nourishing; and when the tumour reaches the fundus by extension from the pylorus, growth becomes luxuriant. “In twenty-three out of twenty-nine examples, the new growth was densest at the pylorus, and had grown thence in the gastric wall towards the œsophagus, in eleven cases infiltrating the whole gastric wall In one case a mass of new growth projected through the pyloric orifice, but in no case was the wall of the duodenum in the slightest degree

* Thin : Cancerous Affections of the Skin.

† Walshe : The Nature and Treatment of Cancer.

affected.”* Cancer of the gall-bladder and common bile-duct is disposed to grow into the liver, and in rectal cancer there is a “tendency to spread upwards rather than downwards.”† “The growth has been known to extend upwards to the transverse colon, transforming all the descending colon into a cancerous mass, while the inferior three inches of the rectum had not suffered the slightest change.”‡ In cancer of the portio-vaginalis and cervix uteri, the lines of growth are less towards the cavity of the uterus than outwards and downwards towards the vagina. Here the looseness of texture in the tissues of the portio-vaginalis may possibly fix the direction of growth, but if the explanation given in this work of cancer of those parts is true, the tissues of the portio-vaginalis and vaginal walls must offer less resistance to growth than the tissues of the body of the uterus.

The relation of growth in tumours to high nutrition is made known by the speed with which cancer kills according as the structure in which it originates is richly or poorly supplied with vessels. Though other circumstances than that of vascularity (moisture, warmth, movement, &c.) make cancer of the tongue more malignant than cancer of the lip, yet the free supply of blood to the lingual tissues is probably one of the causes of the greater deadliness of lingual cancer. It is well known that epithelioma of the scrotum pursues a quieter course than epithelioma of the more vascular penis, and there is often a similar contrast between sarcoma of the skin and sarcoma of osseous tissue with its succulent marrow. The absence of vessels in cartilage is probably the reason why the cartilages of joints are scarcely ever invaded by osseous sarcoma.

Facts of another kind are also at hand in witness of this induction. Writing of mammary cancer, Mr. Bryant has observed “should the breast of a pregnant woman be the seat of cancer, the disease as a rule will progress rapidly, and

* Norman Moore : *Lancet*, vol. ii. 1889, p. 418.

† Walshe : *Op. cit.*

‡ Jessett : *Cancer of the Mouth, Tongue, and Alimentary Tract.*

should the stage of suckling be reached its increase will be still more rapid." And the assertion is confirmed by Gross who says that the growth of cancer under these circumstances "is wonderfully rapid, and its course excessively malignant." The growth-activity is here in relation to the increased nutritive supply of the breast, in the first instance in anticipation of increase of function, and in the second of actual increase of function. A statement of the same tenour has been made by Dr. Matthews Duncan.* "Sometimes, and I think especially in young people, cancer is an acute disease, running its course rapidly. A young lady applied to me on account of slight continued bloody oozing from the vagina; there was nothing unhealthy discoverable except in the posterior vaginal wall a wart the size of half a small pea. It was freely destroyed by caustic. The disease rapidly extended, forming large fixed masses around the lower part of the vagina, and she was dead within three months from the discovery of the wart." Conversely, in very old people when the nutritive processes have become quiescent from lack of vitality, both epithelioma and scirrhus are wont to run a slow and quiescent course. The following cases of Mr. Bryant should be read for their interest in demonstrating the influence of pregnancy and suckling upon the growth of cancer of the breast.

CASE 1.†—"Mr. Annandale reports that he once operated upon a mother and daughter for scirrhus of the breast, both within two weeks; the daughter was nursing when the disease first showed itself, and in her case its progress was much more rapid than in the case of her mother."

CASE 2.—"Mrs. M., aged 35, the mother of nine children and the first eight of which she suckled, came to me in 1868, when she was four months pregnant, with the right breast and skin over it as well as the integument of the chest, side, and abdomen, generally infiltrated with carcinoma. In fact she was skin-bound. The breast with the skin in several places was ulcerated. The right

* Clinical Lectures on Diseases of Women.

† Bryant: Diseases of the Breast.

axillary glands were enlarged, and the right arm cedematous from venous obstruction. The disease in the right breast had appeared as a lump in the gland, which was left after an abscess that formed when suckling her eighth child two years previously. The left breast was likewise infiltrated with carcinoma, and this had followed an abscess after the ninth child ten months previously. This patient died from asthenia about the eighth month of her pregnancy."

CASE 3.—"Eliza W., aged 35, the mother of four children, the youngest being fifteen months, all of whom she had suckled, came under my care in January, 1871, with infiltration of the *left* breast and a brawny condition of skin over it. The disease began three months before, during suckling, as a lump which rapidly grew. The skin over the right breast was mottled and was already becoming infiltrated in lines, probably lymphatic. On March 2nd the woman was sinking."

A mammary tumour carefully observed during treatment by pressure was noticed to increase at the menstrual periods (*Walshe*). Many similar cases of cancer of the breast might be cited. And the effect of the nutritive stimulus of pregnancy and suckling may be seen in cases of mammary adenoma. At page 109 of "Diseases of the Breast," Mr. Bryant reports a case of large adenoma of two years' standing in a patient aged twenty-two, when she was six months pregnant. During the pregnancy the tumour grew fast, as it did during lactation which she carried on with the affected breast for three months. The facts of the following case are remarkable and most instructive.

CASE 4.—"The patient married at nineteen. In due course she had a child which she nursed with both breasts, but had to wean the infant on account of sore nipples. In consequence an abscess formed in the right breast. Within eight months of her first confinement she again became pregnant, and in about the twelfth week she perceived a lump the size of a hen's egg in the axillary border of the right breast. It steadily grew, and on the third day after a natural labour the tumour measured eighteen inches in circumfer-

ence. She nursed only with the left breast, and the right began to decrease in size so that in the eighth month of lactation the growth was not larger than an orange. At this period she became pregnant for the third time, and at the end of the third month as in the second pregnancy the tumour began again to enlarge, but more rapidly. The tumour then measured twenty-three inches. A fourth pregnancy occurred and, as before, the tumour increased. Four weeks after labour the tumour had decreased five inches. Tumour removed; seven years after operation patient quite well and had given birth to three children and suckled them with the breast from which the tumour was removed."

The influence of nutrition increased by the local application of heat is probably illustrated by another of Mr. Bryant's cases:—

CASE 5.—"A woman was induced to put a hot fig-poultice to a tumour in her breast, which had existed for some weeks. The poultice was applied and kept in position for a day, and on its removal I saw the woman. The skin of the breast was then over an area exactly corresponding to that which had been covered by the hot fig-poultice, red and inflamed; to the finger it felt brawny. I suspected at the time that this condition was due to acute cancerous infiltration of the part, and the progress of the case proved the suspicion to be true; for the redness never subsided, and in one week the tuberculation of the skin was marked and characteristic. The case was clearly one of acute cancer, and I believe the local hot poultice hastened its growth."

Pregnancy is also known to act as a stimulus to the growth of ovarian tumours and uterine myoma, and we may be sure that it does so by augmentation of the nutritive processes in the respective organs. At the climacteric when the blood-supply of the uterus is permanently reduced to the lowest point myomas commonly disappear. Again, some ovarian tumours take on a fresh activity with the advent of puberty. Lastly, the relation we have considered is abundantly illustrated and supported by the phenomena of secondary tumours. (See § 38.)

§ 20. *Summary of the General Conditions of Tumour-disease.*

This chapter has introduced us to the causes of tumours in general operation. In reviewing the facts, the primary endeavour has been to place them in their true relations, and secondarily to learn whether there is correspondence or not between the general conditions observed of tumour-disease, and the conditions favourable to histogenic dissolution.

The relative frequency of tumours of the different tissues was seen to be in strict accord with that constituent of our hypothesis which makes neoplasia a form of genesis or true reproduction. The relative rarity of tumours of the highest developmental rank, and the relative commonness of the lowest kinds is no longer mysterious if tumours are the offspring of the tissues. The facts are then seen to be conformable to the general truths of multiplication.

At some length we considered the distribution of tumours among the different organs and remarkable differences of liability were noted. If the induction is true that these differences bear some relation to nutritive supply, and that relative innutrition must be numbered among the causes of tumours, here is further support to the hypothesis of histogenic dissolution. We know from many facts that low nutrition helps to induce histogenic dissolution. Important qualifying circumstances were, however, pointed out, some of which, it was asserted, oblige us to regard low nutrition as a subordinate cause, though it remains a *vera causa*.

Coming next in order for our attention, were the influences of systemic nutrition upon the genesis of tumours. Reasons were submitted for thinking that as an attendant circumstance in the presence of positive factors, high nutrition is favourable to tumour-disease. But it was found expedient to postpone judgment on this point until we have disposed of succeeding divisions of the subject.

The facts as to the age-conditions of tumour-disease, taken in their ensemble, sustain the assumption that the process of tumour-genesis is the process of histogenic dissolution, and the

relations of tumour-growth to nutrition are entirely in unison with the general hypothesis. To sum up the value of the evidence just presented, I think we are justified in saying that, joined to previous testimony, it makes the hypothesis a probable one.

From these general causes of tumours we now turn to those that are special.

CHAPTER IV.

THE SPECIAL CONDITIONS OF TUMOUR-DISEASE.

Tumours of the Lips.—Tumours of the Tongue.—Tumours of the Pharynx, Œsophagus, and Stomach.—Tumours of the Intestines.—Recapitulation and Conclusion.

§ 21. *Tumours of the Lips.*

The preceding chapter has been the means of making known certain factors in the pathogenesis of tumours in general. The more important task now falls upon us to study the peculiarities of tumour-disease as it affects particular parts; we have to inquire how such peculiarities are related to specialities in the local circumstances of tissue-life, and learn to what extent and in what way these circumstances are effective causes of tumours. To include within our grasp whatever may be available in the shape of facts, we must deal carefully in detail with each organic system. It will be advantageous to take first the systems that afford the largest quota of cases, for the commonest forms of tumour-disease have naturally attracted the most attention, and therefore, in connection with them, we possess the richest stores of trustworthy data. We may very well commence with tumours of the alimentary tract, and successively pass on to tumours of the sexual, cutaneous, and other systems.

Epithelioma is the most important neoplastic change to which the lips are liable, and of this disease there is a plentiful supply of examples. At the outset we are met with the fact that the lower lip is much more generally the seat of cancer than the upper. "Cancer of the lip may be said to be confined

to the lower lip, so rare is it in the upper.”* Of 67 cases the lower lip was the seat of the disease in 62.† Out of 160 cases collected by Mr. Jessett‡ the disease was situated in the lower lip in 140, and in the upper in 5, and both lips were involved in 15 cases. In another group of 31 cases,§ the situations noted were as follows :—

Right half of lower lip in 10 cases.			
Left	„	„	8 „
Middle	„	„	9 „
Angle of the mouth (left)	3	„	
Upper lip at junction of lip with gum 1 case.			

This very great proportionate frequency with which the lower lip is attacked is fully corroborated by the observations of others; therefore we need not scruple to attempt to decipher its import. Is this revealed by any connection known to exist between labial epithelioma and the habits of life? It is said that “a very large majority of men suffering from epithelial cancer of the lips are great smokers.” In Winiwarter’s cases nearly all the patients were smokers; there were only about three who did not confess to this practice. From the Middlesex Hospital Reports we learn that “of twenty-four cases in which inquiries were made as to *smoking*, &c., fifteen had been great smokers, and eight moderate smokers; five of the smokers had chewed as well; one had never smoked.” But it is an accepted and almost trite fact that the principal cause of lip cancer is the irritation arising from the use of pipes, and especially clay pipes. Will this explain why the disease commences so frequently in the lower lip? It is plainly one of the reasons. The pipe of the smoker rests upon the lower lip, and it is partly owing to the greater irritation of the lower lip thus entailed that this structure is the common seat of the disease. And if we set

* Holmes and Hulke: System of Surgery.

† Winiwarter: Beiträge zur Statistik der Carcinome.

‡ Cancer of the Mouth, Tongue, and Alimentary Tract.

§ Roger Williams: Middlesex Hospital Reports, 1887.

down, as we justly may, some cases to the co-operation of intemperance in drinking, it is seen that the drinking-vessel of the tippler also rests upon the lower lip. But there are further reasons. The lower lip will be subjected in a greater degree than the upper to the influence of unhealthy buccal secretions. These secretions, which are inseparable from the habits of drinking and tobacco-chewing and smoking, must gravitate to the lower lip and act injuriously upon its epithelium. Then the lower lip is the more mobile of the two lips. Owing to the fixedness of the upper jaw, the lower lip is exposed to greater friction from the lower movable row of teeth.

Of the above-quoted batch of thirty-one cases, the middle line of the lips was the observed seat in nine and the angle of the mouth in three. In connection with these facts, it may be remembered that in smoking the fumes are usually expelled between the lips at the middle line, and it may often be observed that the secretions of the mouth tend to gather about its angles. It testifies to the probable truth of the conclusion as to the influence of smoking, that the disease begins on one side of the lip, and nearly always on that side on which the pipe is held. In a series of more than one hundred cases reported by Mr. Jonathan Hutchinson, there was not a "single instance of symmetrical development of the disease on both sides of the mouth."* And still more remarkable, in three cases of this series the disease recurred, after excision, on the opposite side, the original scar undergoing no change; *but in these three cases the patients held their pipes on the sound side after the operation.*

A fact not to be overlooked, for it consists strikingly with this supposed causation, is the relation of epithelioma of the lip to the sex of the patients. Of sixty-three cases, only one was in a woman.† And of 160 cases only three were in women.‡ Now women as a class are addicted neither to

* *Medical Times and Gazette*, 1860, vol. ii. p. 35.

† Winiwarter: *Op. cit.*

‡ Jessett: *Op. cit.*

smoking nor chewing tobacco, nor are they as intemperate as men. It has happened, too, that some of the female patients have been smokers. In six cases of cancer of the lower lip in women, there was a history of the habit in three, and in the remainder there was no evidence that smoking was not practised.* Mr. Pemberton thus refers to one of his own cases: "It is remarkable that in the only instance in which I have seen the disease amongst women the short pipe should have been the constant companion for seventeen years."†

Inquiries for other etiological factors in the cases of twenty-seven patients resulted in showing that "there was a history of previous *injury* in six, irritation by rough tooth in one, by plate of artificial teeth in one, by scratch from meat hook in one, by holding copper nails in teeth in one, by sting of wasp in one, and by blow from a stone in one case."‡

As a possible cause, adjuvant to those just recognized, dyspepsia should be included, giving rise as it does to unhealthy states of the mouth.

Among the tissue-changes that lead up to labial cancer there must be mentioned chronic sores, cracks, fissures, pimples, and leucoma. In nearly all cases these morbid states probably result from the above-named conditions. They are often maintained for lengthened periods by the original or accessory causes, and only after the lapse of time do they acquire the characteristics of cancer. "Often the disease commences as a small wart or pimple, which the patient is constantly rubbing or picking, so keeping up a constant source of irritation: such a state of things goes on for months, and even years, without any notice being taken of it, until at last the ulcer or warty growth may rapidly increase in size, and the sufferer then when too late seeks advice."§

There is not often any noticeable fault in the general health

* Hutchinson: Loc. cit.

† Clinical Illustrations of Various Forms of Cancer, p. 92.

‡ Roger Williams: Middlesex Hospital Reports.

§ Jessett: Op. cit.

of patients. "Of twenty-three cases in which inquiries were made, the previous health is stated to have been good in twenty-two (with no serious illness since youth in eight), and in one case it had been indifferent."

Lastly, there is the age of patients as a causative condition. Labial epithelioma is "essentially a disease of advanced life, and is exceedingly rarely met with before the age of thirty, and very much more commonly after fifty or sixty years." (*Jessett.*) The mean age in thirty-three cases was 51.8 years. (*Middlesex Hospital Reports.*) Fifty-eight years was the average age in Mr. Hutchinson's cases.

It now devolves upon us to say how epithelioma of the lip can come out of these conditions. If the hypothesis propounded (chap. i.) is true, it should confirm us as to the reality of the supposed factors by making their *modus operandi* intelligible. It must be deemed inadequate unless it can show *how* the agencies, which experience has compelled men to recognize, can induce the pathological state under consideration. We shall find that all these agencies or conditions are comprehended by the conditions of histogenic dissolution (§ 4).

There is first the age of the subjects, and already it has been shown (§ 18) in what manner maturity and senility prepare the way for that cessation of individual tissue-life which histogenic dissolution expresses. Age was said to be a potent *predisposing* cause of neoplasia. This appears specially true of cancer of the lips. Facts put it beyond dispute that in nearly every case there is a special and local incidence of destructive forces. These are the *determining* causes. Smoking, by the nature and long-continuance of the influences it introduces, must tend to shorten local tissue-life. The means by which smoking is believed to be operative is friction of the lip from the use of clay pipes. There is a true and deep analogy between the wearing away by friction of the energies which hold together the units of an inorganic aggregate, and the

wearing away by friction of the energies which hold together the units of an organic aggregate.

Equally prejudicial, and in similar ways, must be the other harmful habits found in association with labial cancer. Traumatic injury means impairment of the vitality of tissue, and so does the chronic inflammation which often leads up to the disease. Inflammation of every form is, in intimate nature, disintegrative and destructive.* In short, the circumstances recognized and acknowledged to be causes are seen, by means of the hypothesis, to be competent causes. The anatomical site of the part—its distance from the central source of nutriment—the ages of the subjects, the prolonged action of the external agents, in association, perhaps, with systemic disorders, are conditions well calculated to induce histogenic dissolution in limited areas of tissue, and reciprocally such weakness in the surrounding tissues that these are unable to contend successfully for nourishment with the newly-created cells. It cannot but be that forces foreign to the life of the organism, and acting daily and even hourly for long periods, will, in certain individuals, be equal to the production of the organismal changes the hypothesis sets forth.

A more extended consideration might be given of the operation of the factors of labial cancer. But in the sections to follow, we shall meet again with similar factors, and then the exposition may be amplified. It ought, however, to be observed here that in most cases the causes act conjointly. The lacerations of a rough tooth may be associated with the friction of a clay pipe, the ulcerations of simple dyspepsia may be kept up by the irritation of an artificial tooth-plate, and so on. Yet varied in nature and in mode of co-operation as the forces at work may be, the morbid effect is uniformly the same. Whether the leading cause is the irritation of a clay-pipe stem, or of copper nails habitually held by the lips, or morbid buccal secretions, there is no variation in the nature of the pathological changes; we have always the same disease. And this, be it

* Cf. *Dissolution and Evolution and the Science of Medicine*, p. 7.

marked, our hypothesis requires, for the causes are assumed to produce the disease by exhausting the vitality of the units acted upon, and not by any special kind of influence.

If we attempt to measure the degree of influence exercised by each agent separately, it appears highly probable that age, constitutional states, and the anatomical site of the disease, are predisposing causes; and that the forces directly incident upon the lips are the determining or actual causes. They are the actual causes in the sense that without them the disease would not be eventual. Much has been made, by earlier and contemporary writers, of the argument that, among individuals, identical conditions of life are not followed by identical effects; that of many men who smoke clay pipes, only a small proportion suffer from cancer of the lips. Against this argument it must first be urged that the abstract proposition, if its postulates were true, may be made of every disease. All do not suffer of those exposed to the infection of scarlet fever. The postulates are not true. The conditions of life are in no two cases identical. The extreme degrees of individual variation in organisms is obvious to the least careful observer in every crowded street. As regards their toleration of noxious influences, men are seen to differ widely. Furthermore, in tumour-disease there is never complete identity in the external conditions. Here this or that agency is greater or less than in the case of another person, and here there is one set of concerted actions, and there quite a different set. It is just in the exceptional cases where the circumstances are approximately the same that the results are approximately the same.

The facts as to the general health of those who suffer from cancer of the lip must be duly dealt with. If the disease at its commencement is related to the whole organism only in a remote sense, and is essentially a local disease bearing witness to the life-experiences of a particular collection of units, then it is not inconsistent that probably two-thirds of the patients

are in good general health when they first present themselves for treatment. At this time deterioration of the general health is not a requirement, according to the hypothetical nature and causation of the disease. Local ill-health may exist quite independently of general or systemic ill-health. Indeed, it is almost certain that cancer of the lip and cancer in some other parts is indirectly consequent upon a vigorous constitution. A state of constitutional weakness would clearly be a bar to the practice of those habits which in most cases are the real determinants of labial cancer. Without a certain lustiness, it would be impossible to indulge habitually and often excessively in the use of alcohol and tobacco. Be it observed, however, that systemic weakness, or disease, considered *per se*, is favourable to local disease. The organism, as a whole, cannot be affected without its parts being affected, which might be illustrated from general pathology indefinitely. And we shall meet with some interesting instances in cases of cancer.

Histogenic dissolution being what it is, its causes will act most effectively if they are slight and enduring. This is the character of the action of both the causes that prepare the tissues and of those that usually determine labial cancer. Age favours the disease because it involves the gradual consumption of the potential energies of the tissues, and such is the local influence of the habit of smoking. (See p. 14.)

We must not omit to note that in labial cancer the tissue implicated in the neoplastic change is the tissue upon which the forces distinguished as causes directly impinge. The new formation is derived from the stratified pavement epithelium of the mucous membrane or skin, and not from the muscular or glandular structures of the lip.

The benign tumours of the lips are chiefly adenoid growths from the mucous glands, and papillomas from the surface papillæ, but our knowledge of their causes is too slight to afford a basis for argument or induction.

Cases Illustrative of the Facts Interpreted.

CASE 6.—“T. W., aged 58, was admitted into the Cancer Hospital on March 5th, 1885, suffering with a large cancerous ulcer implicating the whole lower lip and left angle of the mouth. Has suffered much from gout. Four months ago noticed a small pimple like a ‘boil’ on his lower lip at the left-hand corner, which increased rapidly. Patient is a gasfitter, and *is in the habit of using a brass blow-pipe*. He is also a great smoker. No history of syphilis. Has been rather a hard drinker.” (*Jessett.*)

(This case is selected to show how causes conspire with one another. The age of fifty-eight years, a constitutional disease, the habits of drinking and smoking, and the frequent application of the lip to a brass blow-pipe, all unite, probably, to produce the single effect.)

CASE 7.—“G. H., aged 80. Epithelioma implicating three-fourths of the lower lip. Has been a great smoker, usually smoking a short clay pipe; has frequently burnt his lip with the hot pipe. Fifteen months previously to admission noticed a small pimple on lower lip, which ulcerated, and although he sought advice for this, it continued to increase until it extended along the lower lip to the left angle of the mouth, which became implicated with the disease.” (*Middlesex Hospital Reports.*)

(Here the extreme age and the injurious action of the *short* clay pipe have apparently sufficed to produce the disease.)

CASE 8.—“C. S., aged 60. The left half of the prolabium of lower lip the seat of hard, craggy, epitheliomatous ulceration; the corresponding part of inner surface of the lip also invaded. Two years ago scratched middle of left prolabium with a meat hook; six months later first noticed small hard whitish speck at the seat of the injury. It increased very slowly and remained scabbed over until three months ago; since this time it has spread rapidly. Moderate smoker. No history or signs of syphilis.” (*Middlesex Hospital Reports.*)

(In this case both age and the habit of smoking appear as

predisposing causes and accident is the determining cause. With the tissues prepared by other circumstances traumatic injury precipitates the changes upon which, as we suppose, tumour-disease depends.)

CASE 9.—“Rodent ulcer of the lower lip. S. K., æt. 75, a servant. Has had good health until about thirty years ago, when he got wet through, and since that has been much troubled with his health. He has paralysis agitans of both arms, which he attributes to a severe nervous shock some ten years ago, he being then in great pecuniary and domestic trouble. The ulceration of the lips was caused by a blow received, two years ago, from a man’s fist. This blow cut through both lips, and also made a gash into his nose. Wound of the nose and upper lip soon healed, but the one on the lower lip refused to do so; it remained for two months in this condition. He then went to a druggist, who gave him some lotion to apply, but, after a second two months had elapsed, it began slowly to extend. . . . He had lost all his teeth for nearly thirty years; they came out without being decayed, and he is not aware of ever having been salivated; he has never smoked or chewed tobacco. He has never heard of any of his family ever having had tumours of any kind.” (*Pemberton.*)

(Rodent ulcer is now allowed to be a form of epithelioma. The tangible factors in this valuable example may be thus set down. The age of seventy-five years, and the depressed mental and nervous health, are predisposing conditions. Violence determines the disease. It should be marked that the upper lip healed while the lower remained refractory. This points to some difference in the life-circumstances of the two lips other than the difference which the habit of using tobacco establishes. We are not informed as to the patient’s habits in respect of the use of alcohol; but it has been mentioned that the lower of the two lips is the more exposed to friction and is the more subjected to the action of unhealthy buccal secretions. It is an important circumstance in this case that a lotion, probably an irritant, was applied to the lower lip.)

CASE 10.—“J. M., æt. 64, a labourer, fresh and healthy looking.

Admitted on account of a sore which had formed on the right side of the lower lip. The disease appeared six months since as a small pimple, near to the angle of the mouth on the right side, and was situated close to the junction of the red line of the lip with the skin. He always shaved it off on Sundays until it became too tender for the proceeding. About a month since, after a stimulating application, he found the growth increased, so he applied to the hospital. He can assign no cause for its appearance. He has smoked and has always carried his pipe on that side. His family history is without suspicion." (*Pemberton.*)

(An etiological point of much interest in this case is the repeated injury inflicted at the seat of the disease in the operation of shaving. Cases have been explained by observers as due to wounds made frequently by the razor at one spot. In the present case this was clearly an accessory cause, as also, probably, was the "stimulating application." The essential cause was the use of the pipe; the age of sixty-four years being contributory. It will be noted that the patient was "fresh and healthy looking.")

CASE 11.—"Daniel P., a florid man, aged 52. He was not a smoker, but was accustomed to carry a small brush in his mouth." (*Hutchinson.*)

CASE 12.—"Wm. D., aged 53, a ruddy-looking man who had lived an irregular life exposed to weather of all kinds. The disease had begun a year previously, as a little wart, in the lower lip, at the point at which he used always and for a long time, every day, to carry his short pipe." (*Hutchinson.*)

§ 22. *Tumours of the Tongue.*

With the more inviting region of the tongue before us it will not be worth while to dwell upon the neoplasms of the gums. The primary tumour usually met with in this region is epithelioma, and its admitted etiology differs in no important particular from the etiology of epithelioma of the lip. It will

therefore suffice to quote as follows:—"The disease is of comparatively frequent occurrence, and is usually the result of local irritation, such as that caused by decayed teeth, old stumps, a badly-fitted plate that rubs or pinches the gums in some place, collections of tartar around the teeth, the constant use of neat ardent spirits, burns or scalds; all of these are common exciting causes of the disease."*

The innocent tumours met with in the tongue are mostly lipoma, fibroma, and papilloma; but being comparatively rare little has been observed in connection with the circumstances of their appearance. When not congenital, lipoma and fibroma are generally seen in adults, that is, when the tissues are presumably ripening for discontinuous reproduction. Primary sarcoma is of still greater rarity, and we must look to what has been recorded of the more common epithelioma for material suitable to our purposes.

As in the case of the lips, there is to be considered the part of the organ in which the disease first appears. In a group of eighty cases† the situations of the cancerous ulcers were as follows:—

Root	1
Anterior half of tip	3
Right border	12
Left border	17
Right side	11
Left side	16
Border	1
Dorsum	15
Right underside	2
Left underside	1
Whole tongue	1
	—
	80

* Jessett: Cancer of the Tongue, Mouth, and Alimentary Tract.
† Butlin: Diseases of the Tongue.

The following were the positions in another group of forty-six cases* :—

The right upper surface in	.	.	.	.	12
„ left „ „ „	.	.	.	.	6
„ tip of the tongue „	.	.	.	.	3
„ fore part „ „	.	.	.	.	3
„ right edge „	.	.	.	.	5
„ left „ „	.	.	.	.	9
„ under surface „	.	.	.	.	8
					46

And in fifty-four cases† the positions noted were :—

Right edge (base 9, middle 12, front 1, not stated 3)	.	.	.	.	.	.	25
Left edge	.	.	.	.	.	.	18
Tip	.	.	.	.	.	.	5
Dorsum	.	.	.	.	.	.	4
In substance of tongue (middle of dorsum 1, at base on right side 1)	.	.	.	.	.	.	2
							54

From these tables it may be gathered that the disease is situated in a large preponderance of cases on the edge and sides of the tongue. This fact is too perspicuous to be obscured by those cases where the cancer appears first at other places, and therefore we may with propriety seek its explanation. As in the case of labial cancer, does the clue exist in the antecedents of the lingual affection? First to see what these antecedents are. Numerous observers agree in attributing a considerable proportion of cases of cancer of the tongue to the habit of smoking. Since smoking is proved to be the commonest cause of labial cancer, it may very well be a cause of lingual cancer, looking at the anatomical and physiological relations of the lips and tongue. It is known that smokers are liable to the morbid epithelial changes termed ichthyosis, chronic superficial glossitis, leucoma, and “smoker’s

* Winiwarter: Beiträge zur Statistik der Carcinome.

† Roger Williams: Middlesex Hospital Reports.

patch." In 75 out of 110 cases of chronic superficial glossitis, it was ascertained that only 4 patients did not smoke, 11 simply smoked, 14 did so in moderation, while 46 smoked excessively.* And of these 110 cases, 43 (and probably one more) ended in epithelioma. This is to the effect that the earlier changes in the surface epithelium of the tongue produced by smoking are precursory to cancer in nearly half the number of cases observed. Others unite in recognizing this as one of the antecedents. (*Winiwarter, Butlin.*) Mr. Butlin, remarking upon the point, writes† that "a very large majority of the later cases of lingual carcinoma which have come under my notice have been preceded by an abnormal condition of the surface of the tongue; but if I had not looked carefully for it, I should assuredly have passed it by, believing that the imperfection, the smoothness, the slight bluish-white or pearly appearance of the organ in the vicinity of the cancerous ulcer was a mere accidental complication of the carcinoma not worthy of special notice. The patients, as a rule, are not sufficiently annoyed by the lesser conditions of leucoma, under which name all these conditions are understood, to complain of them, and may be wholly unaware of their existence." Possibly, then, by greater heed to this matter, future observation may show that a still larger percentage of cases of lingual cancer are preceded by chronic superficial glossitis.

It is, I think, a quite warrantable conclusion that smoking is a common cause of cancer of the tongue, and the fact may be at once connected with the circumstance to be explained, namely, that the sides and edges of the organ are the most frequent seats of the disease. The pipe or cigar of the smoker is, with rare exceptions, so held in the mouth that the impact of its point falls not upon the tip, dorsum, root, or under surface, but upon the sides and edges. It is said of "smoker's patch," "In the most typical instances it appears about the middle of the front part of the dorsum, but on one side of the middle line, just where the end of the tobacco-pipe rests, or where the stream of smoke from the pipe or cigar impinges on

* Barker: Holmes and Hulke's System of Surgery. † Diseases of the Tongue.

the surface of the tongue.” The greater friction to which the edges are exposed from contact with the teeth will probably concur with the chemical and mechanical actions of the pipe, and so determine the most frequent outbreak of the disease upon the very edge of the tongue.

In this inference as to the part played by smoking in the genesis of lingual cancer, we are strengthened by its ready coalescence with the facts relating to the sex and age of patients. It affords what we should seek to find, an explanation of the relative liability of the two sexes. Though the exact proportion in which the disease affects men and women is variously estimated by different observers, acceptance may be accorded to the general statement of Mr. Butlin that cancer of the tongue is “incomparably more frequent in males than in females.” In 190 cases, 163 occurred in men and 27 in women.* In 46 cases, 43 were in men and 27 in women.†

Concerning the ages of patients, the records of the London Hospital show that the average age in 190 cases was 52 years, the oldest patient being 79 and the youngest 32; the records of the Middlesex Hospital show a mean age of 53·8 years in 100 cases of cancer of the tongue and mouth.

Thus, in reference to the habit of smoking, these facts are consistent, and the frequency of cancer of the tongue in men is comprehensible. Smoking is almost confined to males, and is chiefly indulged in by young men and adults. The different habits of the two sexes is the meaning, we may be sure, of the relative frequency of the disease in males and females.

But if we give the first place to smoking it is only one of many causes. The following must be included among the causative conditions. Dyspepsia, bad teeth, ill-fitting plates, coarse, hot, and highly-spiced food, chewing tobacco, the use of alcohol, the application of caustics to sores on the tongue, and syphilis.‡ “Of 75 cases in which inquiries were made,

* Jessett : *Op. cit.*

† Winiwarter : *Op. cit.*

‡ Cf. Butlin : *Op. cit.* ; et Jessett : *Op. cit.*

there was history of previous injury in 25; irritation by rough or decayed tooth in 20; other injury in 5 cases. Of 60 cases in which inquiries were made, there was history of previous *disease* of the tongue or mouth in 24; syphilitic lesions in 11; ichthyosis in 11; chronic superficial glossitis in 2 cases, and a wart in 1 case. With regard to *syphilis*, inquiries were made in 72 cases; and in 26 there was distinct evidence of the disease. In 64 cases inquiries were made as to *smoking*, &c.; 39 had been great smokers; 19 moderate smokers; and 6 had never smoked. 10 of the smokers had also chewed." (*Middlesex Hospital Reports*.)

Can these various conditions of lingual cancer be conceived by the help of our hypothesis to effect the pathological changes constituting the disease? Again, as in labial cancer, there is the important circumstance of age. The average age of patients is about fifty years, and the disease is hardly known before thirty. And if we consider the nature and mode of action of the most common, direct, and specific causes, their co-efficiency with age appears to be unmistakable. Tissues that have lived to mature and old age must be by reason of this predisposed to premature dissolution under the constant influence of strong poisons like tobacco and alcohol. The leucomatous patches seen in so many cases to antecede the outbreak of cancer, are probably, when occurring in smokers, simple growths of epithelium excited by the unceasing action of tobacco. Such thickenings may be regarded as hypertrophies or continuous growths having a protective purpose, but requiring for their maintenance such drafts upon the energies of the mucous membrane that at last this may perish by histogenic dissolution. A case of Winiwarter's is cited by Barker as follows:—"The epitheliomatous change had been known to start in a spot of the tongue from which a patient had been in the habit of peeling or shaving off the thickened leucoplakial epithelium due to chronic glossitis." Continuous reproduction having been encouraged to excess, the process ended in discontinuous reproduction and death of the parent tissue.

(Compare Case No. 10 p. 86, and note to Case No. 23 present section.)

Both chronic and destructive, like tobacco and alcohol, are also the local influences of dyspepsia, of hot and highly-seasoned food, of tobacco-chewing, carious teeth, and the ill-fitting plates of artificial teeth. We see that the stress of certain injurious actions must fall especially upon the tongue, and so tend to deplete its remaining stock of constitutional energy. This must be the case not only where tobacco and alcohol are consumed, but where hot foods and drinks and pungent condiments are taken. The tongue, in a greater degree than any other part of the alimentary tract, must bear the brunt of such conditions. Not improbably the use of condiments ranks next to smoking and drinking as a cause of lingual cancer. Some people partake of mustard, pepper, and spiced pickles in quantities that will of necessity be highly exhausting to the mucous membrane of the tongue. I am credibly informed that the disease is frequently seen among agricultural labourers who are accustomed to season their food with excessive quantities of mustard.

In view of these interpretations it is notable that the actions recognized as causes are, as in labial cancer, slight, but persistent: such as are likely not to destroy outright, but to produce that state of ebbing life which is favourable to histogenic dissolution. And when cancer of the tongue supervenes upon ulceration it is not acute but chronic ulceration that precedes the eruption of the disease. The phenomena seen in the transformation of an ordinary ulcer of the tongue into a cancerous ulcer are, I think, made quite intelligible by the hypothesis. "The sore place, no matter what its origin, is at first generally indolent, or having been more or less acute, becomes indolent, and bears all the signs of a chronic sore, discharging little, paining not much, changing little or not at all. If, as is not unusual, it is seated on the border of the tongue, it often stands out on a slightly raised base, or, if it is a fissure, makes its place known by a slight prominence of that part of the border. Either from ignorance on the

patient's part, or from ill-advised treatment, it is irritated, and then slowly enlarges. The surface of the open sore becomes uneven, the fissure becomes deeper and ragged; the surrounding area may become inflamed, but more often is only a little angry. But, and this is one of the most important features of the change, *the surrounding area and the base become slowly and almost imperceptibly harder*, or being from the first indurated, become more and more hard. It is probable that at this time the lesion has already become carcinomatous, for the disease now presents some important characters of carcinoma, of which induration is certainly one of the most important" (*Butlin*). Of these events the first to be marked is the beginning of cancer in ordinary ulceration. Now ulceration is the *complete death* of tissue, and it is a very accordant fact that ulceration should be a forerunner and attendant of neoplasia if this hangs on the vital phenomenon we connect it with. Superficial layers of cells being visibly killed, if the causes persist death will be impending in layers near by, and the units in these layers may at any moment become ripe for histogenic dissolution. The change called induration, which is emphasized by Mr. Butlin as a distinctive feature, may be taken to mark that period when groups of cells break up into new centres and the surrounding parts begin to yield to the multiplying germs.

Besides the causes just considered syphilis is a well-ascertained antecedent of lingual cancer. In what way does syphilis, alone or in conjunction with other conditions, bring on the disease? It works as other causes work by decreasing the contained energies of groups of cells. That it actually causes local death the scars of syphilis are palpable proof. When the cancer starts in the scars of syphilis and the action of the specific poison is in abeyance, the histogenic dissolution can be attributed to the relatively feeble life of scar tissue. The low vitality of cicatricial substance is made evident by its proneness to ulceration and degeneration (keloid) and by its structural imperfection: it never contains the specialized

structures of the tissue for which it is substituted. There is not a little testimony to be hereafter adverted to showing that reparative tissue has a natural tendency to undergo neoplastic degeneration. In singular harmony with this is the statement that "ulcers and scars produced by syphilis are not more prone to become cancerous than the ulcers and scars which are due to any other cause" (*Butlin*).

The general health corresponds closely with that of patients suffering from labial cancer. The patients in nearly two-thirds of Winiwarter's cases were healthy and strong and well-nourished.* Mr. Pemberton remarks that the general health at the outset and for a considerable time after is remarkably good.† "Of sixty-nine cases in which inquiries were made the previous health is stated to have been good in all; and in forty there had been no serious illness since youth." "On admission, 45 patients out of 84 were well nourished and healthy looking; 15 were moderately nourished; 3 were obese; 13 were emaciated; 11 were sallow, and 19 pale."‡

What was said on this head in the preceding section applies with equal force in the present case. If indulgence in tobacco, alcohol, and the pleasures of the table are the chief indispensable causes of cancer of the tongue, it seems to be a necessity that, for the most part, the health of the patients should be robust.

As in the lips so in the tongue, the tissue concerned in the cancerous change is that in most direct intercourse with the assumed causative forces. Epithelioma, that is, cancer of surface epithelium, is perhaps the only variety of cancer met with in the tongue, though there is an abundance of serous and mucous glands in its substance as well as muscular and other tissues. The fact that the tongue does not produce glandular carcinoma is not inexplicable if the present etiological inductions are correct. Mr. Butlin has observed in reference to this point:—"Even if, by and by, it is clearly proved that other varieties of carcinoma do occasionally affect the tongue,

* Op. cit.

† Op. cit., p. 99.

‡ Middlesex Hospital Reports.

the extreme rarity of their occurrence will always remain a puzzle. For the back part of the tongue and the parts beneath the lip are rich in glands, and these parts are very vascular, and the dorsum behind the circumvallate papillæ, although it is not nearly so exposed to injury as the tip and borders, is not by any means protected from injury and irritation."

Cases Illustrative of the Facts Interpreted.

CASE 13.—"C. M., æt. 51, married, by occupation an umbrella maker, was admitted on account of a cancerous ulceration of his tongue. Has generally had good health. Thirteen months since a small sore formed on the tip of his tongue. This caused him little pain, and, though it never healed, it did not increase materially until six weeks back, when, after a drinking bout, his tongue became swollen and painful, appearing to fill his mouth, and the ulceration rapidly extended. Has been a confirmed smoker of short pipes from earliest youth. There is no history of cancer in his family." (*Pemberton.*)

(The facts of this case are forcibly in evidence of conclusions arrived at as to causation, and after the foregoing interpretations it is not necessary to dilate upon them. From its nature we may accept the statement that the ulceration increased after a fit of drinking, and solitary though the fact is, it helps to confirm the belief in the efficiency of alcohol as a contributory cause of lingual cancer.)

CASE 14.—"Mrs. L., æt. 32, a very healthy person of pale complexion, the mother of two children. Three years since she first noticed a small boil on the left side of the tongue. This kept quiet up to the last six months, when it broke and formed an open sore. The teeth in the lower jaw on the same side were long in a state of decay, and have from time to time been removed. There is no history of cancer in the family."

CASE 15.—"Anne W., æt. 33, single. Has had many decayed teeth. Twelve months ago noticed a small wart on the upper

surface of the right side of the tongue. The margin of this speedily became sore, and the ulceration spread. It has spread underneath towards the fraenum, and the margins of the organ are rendered ragged and indurated, and on the right side show the indentation of a carious molar tooth yet remaining." (*Pemberton.*)

CASE 16.—"Caroline C., aged 35, a married woman, and the mother of three children. She was subject to dyspepsia. Cancer on the right side of the tongue. She had broken teeth on the right side of her mouth which had irritated the tongue." (*Hutchinson.*)

CASE 17.—*Cancer of the Cheek.*—"A farm-labourer, aged 49. He was a man of very sober habits, and had never smoked. For several years he had a sharp tooth in the lower jaw which had been liable to prick and irritate the cheek. There was no family history of any malignant disease." (*Hutchinson.*)

(These four examples, easy to multiply, are thrown together to enforce the probability that injury to the tongue from decayed teeth is often, especially in women, the necessary cause. There are, doubtless, co-operating causes left unobserved or unrecorded. But the irritant action is of the usual character, trivial, constant for considerable periods, and definitely localized.)

CASE 18.—A man was admitted into St. Bartholomew's Hospital "with carcinoma of the particular part of the tongue on which his quid of tobacco habitually rested. In this case it is probable that a sore was first formed accidentally, or an excoriation from the constant contact of the quid, and that the ulcer, or excoriation, developed into a carcinoma owing to the irritation produced by the continued use of tobacco." (*Butlin.*)

CASE 19.—"Joseph C., aged 66. The right side of the base of the tongue, the right arch of the palate, the tonsil and adjacent structures, were involved in one mass of malignant growth. He had been a great smoker, and had always smoked with the pipe on the right side of his mouth." (*Hutchinson.*)

CASE 20.—"Male, aged 50. At about middle of right edge of

tongue is a raised oval growth, about the size of half a walnut, which is superficially ulcerated; it feels firm and elastic, and the adjacent part of the tongue is somewhat invaded. The tongue presents numerous patches of ichthyosis and a few small scars of healed erosions. The mucous membrane of both cheeks also affected with ichthyosis. Nine weeks ago first noticed a small sore at about middle of right edge of tongue. Patient attributed it to irritation caused by an adjacent rough decayed upper molar, which was extracted soon after he first noticed the sore. Has been moderate smoker of briar pipe, never chewed. Has had ichthyosis of tongue for several years." (*Roger Williams.*)

CASE 21.—"C. S., aged 49. During the last three years has been subject to small sores on the tongue. Has been great smoker of clay pipes, and has sometimes chewed. Well nourished and healthy looking. The upper surface of tongue presents several small erosions, and small scars and patches of tessellated ichthyosis. On the mucous membrane of each cheek are several ichthyotic patches. On the under surface of the front part of the tongue, on the right side, is a flat eroded cauliflower-like outgrowth, the size of an almond." (*Roger Williams.*)

CASE 22.—Male, aged 52. "The whole of the upper surface of tongue is corrugated and fissured and scarred as from old syphilitic disease. At the under surface of the tongue, on each side, and involving the adjacent part of the floor of the mouth, are several irregular ulcerated patches. Has been subject to ulcers of tongue and mouth for the last three years: during the last three months several of these have become indurated and increased in size. Old syphilitic disease of the tongue, &c., for several years; has been a great smoker of clay and wood pipes." (*Roger Williams.*)

CASE 23.—"John C., aged 50, a bronzed, wiry, healthy-looking labourer from Hampshire. He had a long, narrow, trough-like ulcer on the left half of the upper surface of his tongue, reaching nearly from its tip to within a short distance of its base. The edge of the ulcer was rugged and indurated, and both it and the base were in some parts beset with coarse granulations, and in others coated with sloughs. On both lateral surfaces of the tongue, and on the unulcerated right half of the dorsum linguæ, were several tough and less flexible patches, whitish and buff-coloured.

The patient said he had had these white fibres on his tongue many years." * (*Hulke: Medical Times and Gazette*, 1873, vol. i. p. 135.)

CASE 24.—“About three years after this, my fireman, who had had these apparently harmless plaques on the tongue during nearly twenty years, returned to me with a characteristic ulcerated epitheliomatous knot in the dorsum of the tongue, which ended fatally in a few months.” (*Hulke: Loc. cit.*)

(This group of cases illustrates how cancer of the tongue may be causatively associated with the use of tobacco, with chronic ulcerations, chronic superficial glossitis, and syphilis. Where the causes of the precancerous states, chronic glossitis and chronic ulceration, are left unassigned, we may still believe them to be sequential to external irritation of one kind or another.)

CASE 25.—Epithelioma of the gum. “An edentulous old farm-labourer. He had a small oblong tumour in the gum clothing the shrunk alveolar process of the left upper maxilla, above the lower lateral incisor, *his only remaining tooth*. . . . The patient’s account of it was that the tumour began twelve months before as a small sore, caused, he thought, by the fretting of the gum by the lower tooth.” (*Hulke.*)

§ 23. *Tumours of the Pharynx, Œsophagus, and Stomach.*

There has been recorded a very limited number of facts relative to the conditions of tumours of the pharynx and œsophagus. This is owing partly to the comparative infrequency of tumours of this division of the alimentary canal; partly to the inaccessible situation of the œsophagus; and partly to the fact that until quite recently medical observation has not been much directed to the environment of the individual patient. That we possess the information we do of the circumstances of labial and lingual cancer must be

* Microscopic examination proved these leathery patches to be “essentially overgrowths of the epithelial and papillary tissues.”

attributed to the prevalence of the disorder, and to the ease with which the pathological changes are observed, rather than to a due appreciation of the principle that we should look to the investing forces for the true causes of a disease. Cases of cancer of the œsophagus have, however, supplied some data that deserve more than a passing notice.

This disease has been met with in all parts of the canal, but opinion differs as to which parts are most frequently affected. From an examination of the results of several observers I have little doubt that the usual seats are the upper and lower thirds and a point at the bifurcation of the trachea, and that the frequency diminishes in this order. We read that “undoubtedly in by far the larger number of instances the disease occurred in the upper than in the middle or lower thirds.”* Again, “Cancer of the œsophagus occurs most frequently at the upper end of the canal behind the larynx; most rarely at its middle part.”† Of Dr. Winiwarter’s eight cases, in three the seat of the disease was the cardia and cardiac end of the œsophagus, and in four it occupied the upper third.‡ According to Ziegler, “It may appear at any point of the tube, though it is most frequently met with in the lower third.” If, as is most probably the case, the beginning and end of the œsophagus are the ordinary situations, how may we explain the fact? That the work the organ is required to perform decides the liability of the two extremities. Whatever passes through the viscus either as food or drink will come into most intimate relation with its tissues at the upper and lower divisions. These are the narrowest parts of the canal, it “being most contracted at its commencement, and at the point where it passes through the diaphragm,”§ and here the functional strain will be concentrated. And at the pharynx, and junction of the pharynx with the œsophagus, there are the most active muscular contractions upon the

* Butlin: *Sarcoma and Carcinoma*.

† Walshe: *The Nature and Treatment of Cancer*.

‡ Beiträge zur Statistik der Carcinome.

§ Gray: *Anatomy, Descriptive and Surgical*.

substances ingested, a fact which may be connected with the large number of cases where the disease commences in the upper part. Also, at the position of the tracheal bifurcation a pathological narrowing of the œsophagus is probably often occasioned by bronchial dilatation. Thus, in the absence of positive knowledge of the life-conditions of patients, it may be conjectured from the common seats of the disease that it has an etiology similar to the etiology of lingual cancer. If this conjecture be entertained we find additional support for it. Mr. Jessett, of the Cancer Hospital, writes:—"I have very little doubt that the habit of taking very hot substances or pungent sauces, such as chilies, mustard, &c. in large quantities, may, by constant irritation in a subject predisposed to the disease, form a class of causes which may excite the disease."

We know that cases have been ascribed to injury caused by drinking corrosive poisons, and to the cancerous degeneration of cicatrices, as of burns or syphilis. But facts leave no room for doubt that the misuse of alcohol is frequently the essential factor. (See appended cases.) In sixty cases observed by Sir Morell Mackenzie,* "five patients acknowledged to have been free drinkers, and four others were publicans by occupation." And the opinion of Gyser is quoted that "the insane craving of delicate people for spirits being gratified for many years, is the primary cause and originator of those indurated rings (of the œsophagus), and of the miserable death which results from them." Most of the examples of the disease, too, are in the less temperate males. Of fifty-four cases tabulated by Mr. Butlin, four-fifths occurred in men. There were seventy-one males and twenty-nine females in the hundred cases collected by Sir Morell Mackenzie. Next, it appears probable that the lower classes, who have coarse habits of eating and drinking, are specially subject; the cases in Mr. Butlin's table were mostly drawn from the humble classes. Furthermore, if we may infer anything as to causation from the nature of the neoplasm, the opinion we have hazarded is

* *Medical Times and Gazette*, 1876, vol. i. p. 649.

additionally sustained. Epithelioma is the usual form. "Carcinoma of the upper part of the œsophagus is generally pure epithelioma" (*Winiwarter*). In fifty-eight cases only four were of the spheroidal celled variety (*Butlin*). Thus, as in the tongue, it is the surface epithelium that becomes diseased, that is, the tissue upon which the force of the irritant action must chiefly fall.

Respecting the influence of age, the data are such as we met with in cancer of the tongue and lips. Out of fifty-four cases there was not any patient less than thirty years of age, and half the cases belonged to the period of fifty to sixty-five.*

The interpretation of the conditions of pharyngeal and œsophageal cancer is the interpretation of the conditions of lingual cancer. The abuse of alcohol, tobacco, condiments, hot beverages, rough eating, and injury, in conjunction with age, would establish the neoplastic change in the manner already fully expounded.

Of the conditions of the benign tumours of the pharynx and œsophagus it is difficult to obtain any usable data whatever, so that we must needs pass on to other fields.

We are hardly better off for information as to the habits and circumstances of patients who have suffered from tumours of the stomach, although the mortality from cancer of this organ is very large. In the reports of cases it is quite exceptional to find that any attention has been given to the dietetic habits of the patients. Tumours being almost everywhere believed to come spontaneously, it is not thought needful to obtain the kind of information that is valuable beyond any other, but often great labour is expended in obtaining and collating material not to the purpose.

The benign tumours of the stomach are lipomas, myomas, and fibromas, but they are of rare occurrence. Mucous

* *Butlin*: Op. cit.

polypi are found in association with gastric catarrh, which is a destructive change.

In connection with the seat of cancer of the stomach there is the definite and reliable fact that the orifices are the most common seats of the disease. Dr. Brinton's researches show that the orifices are attacked in 71 per cent. of cases.* And in 1848 cases the pylorus was affected 1110 times.† Here, again, as in other segments of the alimentary canal, neoplasia occurs where the action of incident forces is intensified. Since at the cardiac and pyloric orifices the sectional area of the viscus is much diminished, any harmful properties, either in the way of quality or excess, in the contents of the stomach, must exert an undue effect at these contracted parts. If the facts be explained in this way we are helped to further understand why the pylorus is far above all other places the favourite seat. During the period of gastric digestion, when the pyloric aperture is closed, the vermicular movements of the stomach will be mainly towards the intestines, and but little towards the œsophagus; hence will the strain of function be felt more at the pylorus than at the cardia. And the tendency to a transverse form of growth in pyloric cancer is in harmony. The causes being what we suppose, their action will tend to be distributed upon all parts of an annular area. Reasoning thus, from structure to function, we are upheld by the evidence of gastric irritation preceding the open declaration of cancer. Dyspepsia is an early and the usual precursor. "It is undeniable that cases of gastritis are observed, which finally end, after several years, in cancer."‡ "In cases of cancer there is very commonly a history of dyspepsia perhaps from youth."§ There are some significant observations by Dr. Brinton on this point. He says:—"In some, symptoms absolutely those immediately preceding death (pain, vomiting, &c.) have occurred intermittingly, for ten, fifteen, seventeen, twenty years before." "In others, the first and last attack has been

* Lectures on Diseases of the Stomach, 1864, p. 230. † Jessett: Op. cit.

‡ Ziemssen: Cyclopædia of the Practice of Medicine.

§ Coats: Manual of Pathology, p. 550.

of but a few weeks' duration. In both classes the necropsy has shown the whole or part of the cancer to be so shrunken, hard, or even stony, as to refer its origin to a date at least many months prior to the last illness."* But that improper alimentation is one of the causes is shown in a positive manner. The disease is common among publicans and others who consume much alcohol. Cases have also been connected with the habit of drinking vinegar to prevent or remove obesity. It is said that the inhabitants of the Haouai Islands use an acid liquor called kava, for the purpose of preventing corpulence. This liquor causes suffering in the epigastrium, and the kava drinkers perish in a state of marasmus. I think we may suspect that here cancer is the direct effect of an improper article of food.

Of all the indirect testimony perhaps none is of greater cogency than the concomitance of simple ulceration of the stomach with cancer. In many cases the appearances after death forcibly suggest the beginning of the disease in chronic ulceration, or in the decay of old cicatrices precisely as happens in the tongue. The scars of ulcers "are often found in stomachs which have subsequently been attacked by the deadlier malady." "The coincidence of the open ulcer with cancer is scarcely less frequent. But, as might be expected, in these cases also it is the cancer which is added to the ulcer; and never *vice versâ*—the ulcer to the cancer. An ulcer, for example, which has lasted many years, suddenly ends in death—the necropsy revealing a considerable cancerous infiltration in the thickened margin of the ulcer, or in that more chronic thickening of the walls of the stomach which often extends some distance beyond this margin, or showing a fungus mass of comparatively recent growth, springing up from the centre of the excavation."† It may also in rare instances involve the parietes of a chronic abscess caused by perforation.

Now ulceration of the stomach is a disease impossible to

* Op. cit., p. 216.

† Brinton : Op. cit., p. 242.

dissociate from faults in the alimentary conditions. Besides the character of the lesion, which palpably evidences destructive action, the patients are often known to be intemperate in the use of alcohol or indiscreet in the use of food. Says Dr. Brinton:—"Many of the middle-aged subjects of this lesion are persons of intemperate habits. The sufferers from this disease find their symptoms greatly aggravated by copious meals; by animal food; by hard, tough, and indigestible substances; by hot food or drink; and, lastly, by irritant substances. While, conversely, the use of bland, moderately-azotized food of soft, pulpy consistence, at a cool temperature, and in small quantities, not only relieves the symptoms, but often, if steadily persevered in, completely cures the malady." In other words, the effects cease, the causes being removed.

Such indications as the slender array of facts supplies are to the effect that the life-conditions of the individual organ are the influences which set up the disease, and if we tentatively accept this conclusion the less regular and healthful gastro-nomic habits of the male may be paired with the greater frequency of the disease in men. Out of 784 trustworthy cases collected by Dr. Brinton, 440 were in males, and 344 in females; but a greater disproportion is shown in the results of other observers. According to Dr. Habershon, twice as many men as women are afflicted. Strain, then, resulting in exhaustion of the proper structures of the viscus, appears to be the essence of the disease, and this exhaustion is related in the causative sense to age and excesses in the quantity of food ingested, or to defects in its quality. In six hundred cases the average age at death was fifty years. It emphatically countenances this view that gastric cancer is probably in all cases glandular, being either scirrhous, cylindrical-celled, medullary, or colloid carcinoma. The parent tissues of the new growth are the specialized cells of the stomach, the cells concerned in its proper work, and these are the cells which, according to our argument, perish by histogenic dissolution. It will not have escaped the penetration of the reader that the

evidence presented exhibits the causes, taken in their totality, as long-continued actions of moderate degree, such as we have seen obtains in cancer of the higher parts of the alimentary canal, and such as has been shown to be favourable to histogenic dissolution and low tissue-resistance.

Cases Illustrative of the Facts Interpreted.

CASE 26.—*Cancer of the Palate.*—"A stableman, aged 68. The entire left half, and the hinder part of the right half, of the hard palate were occupied by a slightly tuberos, ulcerated, papillose excrescence. The velum palati was also swollen, stiff and knotty. The patient related that twelve or thirteen months before, a child which he held in his arms whilst he had a pipe in his mouth, struck its hand against the bowl of the pipe, and so caused the other end of the pipe to stick into his palate, making a little wound, which for a few minutes bled freely. Before this accident he was not aware of anything wrong in this part, but one month afterwards he found that a small wart had grown up from the wounded spot. In two months this had, he said, attained the size of a halfpenny. He became alarmed, and went to a hospital, where he was advised to have it cut out; but he would not make up his mind to this till four or five months later. Meanwhile the excrescence constantly increased. Its excision was shortly followed by the appearance of a fresh warty growth. This also was excised, and a second recurrence soon occurred. He survived until the following November, the cancer accomplishing its course in about sixteen months from the time it was first noticed." (*Hulke: Medical Times and Gazette*, 1873, vol. i. p. 135.)

(This instance is cited principally to show that what may be a determining cause in one case becomes predisposing in another. Here the habit of smoking unites with age to prepare the tissues for changes which an accident sets on foot. In view of its bearing on the prophylaxis of cancer, it may be profitable to surmise that if the palate of this patient had not been wounded he might have passed through life without suffering from cancer of this part; or that, had he not indulged in the use of tobacco and yet had sustained a wound of the palate he might still have escaped.)

CASE 27.—*Cancer of the Pharynx*.—"The patient, a healthy-looking, well-nourished woman, aged 33 when she died, did not live more than seven months from the first appearance of the disease. For three or four months the symptoms were chiefly those of a cold in the throat and windpipe, slight huskiness of voice, clear white expectoration, soreness of different parts of the throat, slight dysphagia. The disease did not involve the œsophagus, but greatly contracted the lower part of the pharynx, with a villous growth." (*Hunter*.)

(In the lack of information as to possible causes, the report of this case may be placed with the majority of reports upon cases of cancer of the pharynx. It is adduced here to serve as an example of cases that apparently supply no evidence of perceptible cause. We ought not to fall into the error of drawing positive conclusions from such negative evidence. We cannot say that the disease was related to any form of irritant, nor can we say that it was independent of conditions of this sort. Judgment must be suspended. It is, however, made probable by the fuller information furnished in other cases that a full knowledge of this patient's environment would disclose an etiology reconcilable with our hypothesis.)

CASE 28.—*Cancer of the Œsophagus*.—"C. W., aged 39 years, a cooper, formerly engaged in the wine vaults of the St. Katherine Docks. His family history was good, there being no trace of any malignant predisposition. He was married, and the father of eight children, of whom five were alive and strong and healthy, except one who had had some disease of the hip. Patient himself had never had any serious illness; he never had syphilis. Three years before he suffered from sickness and vomiting in the morning before eating, but this passed off without any special treatment. About six years before admission he had been in the habit of drinking about half a pint of brandy a day; this he continued to do until the attacks of sickness mentioned, but after that had restricted himself to malt liquors. He had never had any accident or swallowed any corrosive fluid, and knew of no cause for the complaint from which he was suffering when admitted. For some years he had had winter cough, which usually left him in the

spring. Eighteen months before admission he began to loose flesh, and felt weak and languid, and had no appetite. Nine months afterwards he first noticed some difficulty in swallowing solid food, and after a few weeks all solid matter which passed into the œsophagus was rejected, so that nothing but fluids passed into the stomach. At the *post-mortem* examination, it was found that just opposite the left bronchus the œsophagus was embedded in a mass of cancerous growth." (*Couper : Medical Times and Gazette*, 1880, vol. i. p. 461.)

(The value of this case lies in the clearness of the evidence as to causation. The patient was of healthy antecedents, and prior to what may be regarded as the onset of the disease that destroyed him had never suffered from serious illness. Upon this foundation cancer of the œsophagus was instituted, and, I think, no hesitancy need be felt in saying that it was instituted by the ingestion of alcohol. If alcohol, as we know assuredly, can wipe out of existence the parenchymatous cells of the liver, or the parenchymatous cells of nerve-tissue, we may be confident that under appropriate circumstances it will effect such a reduction of the vitality of a part as we have assumed for the process of neoplasia.)

CASE 29.—*Cancer of the Œsophagus opening into the descending aorta.*—"J. G., aged 62, a labourer. He is of spare habit, much emaciated. All the family are very healthy. One brother died from 'drinking too much.' He worked as a biscuit maker till he was thirty, and since that time as a common labourer, at any kind of work. *There is reason to believe that his habits have not been very temperate.* He states that he has never drank any hot or corrosive fluids, being accustomed to drink his tea, &c., nearly cold." (*Davies : Medical Times and Gazette*, 1860, p. 637.)

CASE 30.—"Mr. J. L., æt. 84 at the time of his death, had for upwards of forty years had a difficulty in swallowing food. He thought it originated in a habit of eating fast. In consequence of this difficulty of deglutition, all the solid food he took was divided into very small portions. In the last twenty years of his life, whenever he happened to eat a morsel exceeding a certain size (and

that very minute), it lodged in the œsophagus, and for several days, or even more than a week, he would take neither food nor drink. He was not known to suffer from sickness, nor did he ruminate or bring up his food in pellets. He never had a bougie passed down his throat. He indulged to excess in the use of spirits.

“At the autopsy the only parts in which any disease was found were the œsophagus and certain structures in its immediate neighbourhood. The specimen itself displays epithelioma of the œsophagus, with ulceration and affection of a lymphatic gland. But below the part which is the seat of cancer the œsophagus is greatly narrowed, and here there is no indication of any change beyond a simple stenosis. It has, therefore, appeared to me and to others to whom I have shown the preparation that the epithelioma has probably been of comparatively recent development, and that the long-standing dysphagia was caused by the narrowing of the cardiac end of the œsophagus.” (*Hilton Fagge: Guy's Hospital Reports*, vol. xvii. 3rd series, p. 413.)

(Whether Dr. Fagge's interpretation of the sequences of this case is the correct one or not there are facts enough to account for the local neoplastic changes. For forty years there was some perversion of function in the part, and the patient was in the habit of taking spirits to excess. If the stenosis of the cardiac end of the œsophagus was the primary lesion, the lodgment immediately above of ingested matters would be an efficient cause of the neoplasm in a subject eighty-four years old.)

CASE 31.—“J. R., æt. 45. He was a married man, a labourer, and intemperate in his habits. At the commencement of the œsophagus extensive ulceration was found on inspection; the ulcer was four or five inches in length, irregularly tubercular on its surface, and several tubercles were situated in the mucous membrane, both above and below the ulceration.” (*Habershon: Diseases of the Abdomen*, p. 94.)

CASE 32.—“G. E., æt. 73. He was a table-cover maker, and in his early life had been intemperate. Eight months before his admission he received a severe fall, from which he never recovered; and two months later he began to suffer great pain in eating solids, and he had occasional attacks of vomiting. These attacks became

more and more frequent, and latterly almost incessant. At the central part of the œsophagus, opposite the root of the lung, there was a large irregular ulcer, two inches in length, which involved the whole of the tube." (*Habershon : Op. cit.*)

CASE 33.—*Medullary cancer of the Œsophagus. Chronic Pneumonia.*—"W. G., æt. 69, had been an attorney, but he had become reduced in circumstances. For twelve months he had had cough and shortness of breath, sometimes palpitation of the heart, but no hæmoptysis. There was evidence of old disease at the apex of the right lung, and acute bronchitis with it; with these were associated tolerably clear evidence of organic disease of the œsophagus, probably cancerous. On inspection, the lung was found to be very firmly adherent to the right apex, and a thick dense layer of fibrous tissue was with great difficulty separated; the whole of the right pleura was destroyed. The lower lobe of the left lung was also pneumonic. In the œsophagus was an ovoid mass, about six inches in length and one in thickness, attached at the root of the lung, and reaching nearly to the cricoid cartilage." (*Habershon : Op. cit.*)

(The co-existence of œsophageal cancer and pulmonary disease is not infrequent. In the present case it is presumable that the morbid state of the lungs and the morbid state of the œsophagus were associated in two ways. They probably had a common origin in the conditions of the patient's life, which we may suspect were gravely at fault; and dilatation of the bronchi may have determined the seat of the cancer by compression of the gullet.

It was pointed out at page 84 how diseases or conditions of life prejudicial to the vitality of the whole organism must of necessity favour neoplasia *in the presence of its essential and local causes*. This is one among the many cases we shall meet with illustrating the fact. Note how exactly coincident is the experience of Dr. Brinton. He says: "I have witnessed misery, anxiety, and starvation, suddenly rouse into fatal activity a gastric cancer: and that, this cancer having run its course in a few weeks, the necropsy has verified anatomical details conclusively proving that it must have been present as

an unsuspected tumour for months, or even years, during which the patient has literally enjoyed the most robust health.” (*Op. cit.*, p. 261.) Interpreted by our conception of neoplasia these facts teach us that locally incident actions having slowly wrought their due consequences in the gastric tissues, new circumstances distressing to the whole organism further the growth of the neoplasm in the first place by weakening the “physiological resistance,” and, in the second place, by promoting the established local process of histogenic dissolution. We have seen, p. 46, that in tumour-masses all nervous connections have been severed, and therefore the vitality of the *tumour-units* cannot be immediately depressed by misery and anxiety. Observe, however, that the *tissues* with which the tumour must contend for life are still under nervous influences and their vitality is depressed by misery and anxiety, and such depression in these as yet integrated tissues will favour further disintegrations by histogenic dissolution.)

CASE 34.—*Cancer of the Stomach.*—“J. H., æt. 68. Patient had an attack of ‘liver complaint’ thirty years ago, with symptoms resembling his present attack, *i.e.*, pain in right hypochondrium, feverishness, and high-coloured urine. He was laid up about six weeks. He has been in the habit of drinking from three to five pints of beer daily. About three months ago his appetite and strength began to fail and he suffered from epigastric pains. These symptoms have become aggravated. *Post-mortem*, the liver was found densely infiltrated with new growth. A cancerous growth, the size of half-a-crown, was situated on the posterior wall of the stomach in the greater curvature, two inches from the cardiac orifice.” (*Pasteur: Middlesex Hospital Reports.*)

CASE 35.—“P. S., æt. 52. Has been a free drinker, but generally healthy. Carcinoma of the pyloric end of the stomach.” (*Ibid.*)

CASE 36.—“M., æt. 45. The patient has been a heavy beer-drinker. Five years ago he vomited a large quantity of blood and passed blood per rectum, but recovered completely. Six months ago he wrenched his left side whilst lifting a heavy weight; since that time he has been getting gradually weaker, suffering a good deal

from abdominal pains and constipation, and from slight jaundice. Three months ago his attention was drawn to a 'lump' in his abdomen, at the seat of the original pain. Autopsy. The pylorus is surrounded by an irregular ulcerated mass of cancer, which infiltrates the coats of the stomach for one inch, and extends along the duodenum for about one and a half inches." (*Ibid.*)

CASE 37.—*Villous growth of the Stomach. Cirrhosis. Ascites.*—"J. D., æt. 65, was a married woman who had been accustomed to take spirits, but she stated that she had been in good health till six months previously, when she caught cold, which was succeeded by cough, by shortness of breath, and by burning pain at the scrobiculus cordis. Seven weeks before admission, her legs, and afterwards the abdomen, began to swell; diarrhœa, great prostration, and syncope came on, and before death she became partially comatose. On inspection there were adhesions between the liver, colon, and stomach, and the peritoneum contained about a gallon of serum. The liver was in a state of advanced cirrhosis. The stomach was moderate in size, flaccid, and in the inner aspect of its anterior wall presented a large villous growth, about three inches in diameter, the edges of which were raised, and the centre ulcerated." (*Habershon.*)

(Here, in this batch of cases, is shown the association of intemperance and cancer of the stomach. That the association is one of cause and effect cannot, I think, be doubted. In the last example the alcohol consumed had produced complete dissolution of the hepatic gland-cells and in the gastric gland-cells that partial dissolution we conceive to be the root-change in neoplasia. It is also worth marking that "with the exception of burning pain at the stomach two months before death there was no sign observed of the disease of the stomach." Thus, the absence in cancer of the stomach of symptoms referable to the organ itself does not prove the absence of pathogenic influences.)

CASE 38.—*Cancer of the Stomach associated with tubercular disease of the Lungs.*—"F. G., aged 60, a 'painter's jobber.' When admitted the man was emaciated, pallid, with dropsical legs, and complaining of a 'troublesome cough, worse at night.' His then illness was of

eight or nine weeks' standing; but he had been ailing long before. . . . Death took place from exhaustion and general dropsy. He retained throughout an excellent appetite, and was placed successively on broth diet, fish diet, and ordinary diet; he then had milk diet with a chop; and was particularly fond of gruel, of which he ate largely on the day of his death. The upper lobe of left lung was found to be profusely studded with grey miliary tubercles. The stomach which was firmly adherent to the liver, to the spleen, and to the transverse colon, was of normal size. Its walls, with the exception of the extreme fundus and the pylorus itself, consisted of a hard unyielding substance about three quarters of an inch in thickness, the internal surface of which was in a state of uniform ulceration. On section this structure was found to occupy all the coats of the stomach, except the peritoneal, which was unaffected." (*Coote: Medical Times and Gazette*, 1859, p. 377.)

(This instructive case exemplifies the not uncommon concomitance of gastric cancer and phthisis. Just now we considered a case where cancer of the œsophagus co-existed with extensive disease of the lung, and a suggestion was made as to the probable significance of the association. What was then said applies, I think, in the case above. I have elsewhere submitted the theory that ordinary pneumonia and phthisis are intimately related to the alimentary conditions of the organism.* Gastritis is a frequent accompaniment of phthisis, and we have seen that it is the common antecedent of cancer of the stomach. Writing of chronic gastritis Dr. Habershon remarks: "The cause of this condition appears to be persistent congestion; but, it may also arise from long-continued excesses, and it has been observed especially in tuberculosis as well as in phthisis. . . . Of one hundred stomachs examined twenty-one had acute catarrh, nineteen chronic catarrh, and in seventeen the two states were combined." The notes of the case we are contemplating speak to the free ingestion of food even at the point of death. I do not think there is much doubt that here cancer of the stomach and phthisis were the joint products of gastronomic excesses, understanding by the word "excess" an excess relative to the organic powers of the individual.)

* *Dissolution and Evolution and the Science of Medicine*, p. 154, *et seq.*

CASE 39.—*Chronic Ulceration of the Stomach. Cancer.*—"J. T., æt. 46, a weaver, who had been living at Spitalfields, was a regular and sober man, but he had been a great smoker. For thirty-four years he had been employed at the loom, and he had suffered much from the shuttle striking the scrobiculus cordis; these blows at first produced nausea and faintness, which continued for several hours. Five hours before admission the same unpleasant symptoms returned, obliging him to discontinue his work; they were accompanied with vomiting, although at first only his breakfast was rejected. Six months prior to his appearance at Guy's he was again attacked with pain and vomiting. . . . The vomiting continued very severe, and he became increasingly prostrate; hiccough came on, coffee-ground vomiting, and he gradually sank.

"On opening the stomach, an oval ulcer about two and a half inches in length, and one in breadth, was observed surrounding the constriction; its edges were rounded and elevated; its base quite smooth. . . . In the omentum were several hard tumours, and the omentum itself formed a firm, contracted mass, about the size of the middle finger. . . . The growth closely resembled chronic ulcer in its general and microscopical appearance, except that it nearly surrounded the pyloric extremity." (*Habershon.*)

CASE 40.—*Diffuse Colloid cylinder-celled epithelioma of the Stomach originating round the entrance of the œsophagus.*—"Patient was a stone-mason, aged 33 at the time of his death, and for some years he had worked at a lathe for turning sandstone. In following this occupation, it was necessary for him to stand nearly all day pressing a long iron chisel resting heavily against his left hypochondriac region. To this and the fact that for a lengthened period he had to live upon carried meals, he and his friends were inclined to attribute the origin of his illness. In the spring of 1887 he was confined to the house for a week or two with symptoms of acute or sub-acute catarrh of the stomach, his digestion having been weak for some time previously." (*Lindsay Steven.*)

(Though in the first of these cases the existence of cancerous changes in the stomach was not established microscopically, the likelihood of their presence is considerable. In both cases long-continued external actions were probably largely concerned in producing the disease.)

§ 24. *Tumours of the Intestines.*

If we now glance at the remaining divisions of the alimentary canal, cancer is again seen to be almost the only important form of neoplasm. And the facts that have been registered as to its conditions are of the same order as the facts relating to the conditions of cancer of the stomach, œsophagus, and mouth. The points most exposed to irritation of whatever kind, to injury, and functional excess, are out of all proportion most liable to suffer. In primary cancer of the duodenum, a frequent place of origin is the opening of the bile-duct where any unhealthy changes in the quantity or quality of the bile must first be unfavourably felt. Very often cancer of the duodenum is secondary to cancer of the liver, and in numerous cases a causal relation has been established with irritation from the presence of gall-stones. As regards the rest of the small intestine the jejunum and ilium are affected extremely rarely, and they are the least exposed to harmful actions.

In the large intestine cancer is nearly confined to the cæcum, sigmoid flexure, and rectum. Out of forty-five cases of stricture of the intestines occurring at Guy's Hospital, twenty were of the rectum and ten of the sigmoid flexure. We know by the frequency with which the fæces become stagnant at the cæcum, and its liability under these circumstances to inflammation and contusion, that the life-conditions of this structure will account by our hypothesis for its being the occasional seat of cancer. (See appended cases.) The conditions are similar at the sigmoid flexure and rectum. Whatever substances form the indigestible residue of food, will come most directly into contact with the intestinal mucous membrane at these situations. And if the mass of the fæces is habitually unduly great, or the quality of them unhealthy, there will result excessive functional excitations of the lower parts of the large intestine, for here the fæces are most liable to be arrested in their onward passage. The conventional habits of modern social life require that the fæces should

remain much longer in contact with the rectum and sigmoid flexure than with any other portion of the bowels. The extreme frequency of rectal cancer may be connected with the fact that it is the terminus of the gut. Here fæces must be retained until opportunity serves for their discharge, but elsewhere in the intestines they are ever at liberty to move onward in the direction of the outlet. It agrees in a remarkable way with this explication that rectal cancer begins not at the very end of the bowel, but where the fæces are retained, about one and a half inches within the external opening. "Excepting where epithelioma had begun in the skin around the anus, or at the junction of the skin with the mucous membrane, or in the female genital fissure, and had spread from hence into the rectum, I do not call to mind a single instance of cancer affecting the rectum where there was not such a free space of healthy mucous membrane between it and the anus."* (See case 45.) It further agrees that the neoplasm takes origin from the glandular elements of the mucous membrane, the bodies whose function it is to lubricate the fæces. These elements, presumably exhausted by undue excitations, dissolve into new centres of discontinuous growth.

Others have attached much importance to mechanical irritation. "The cause of cancer of the rectum must be ascribed to a great extent to local irritation; from its situation it is not surprising that it should be a favourite seat of the disease. In one case that came under my notice a short time since, on examination a quantity of fish-bones were found mixed with the fæces in the rectum, causing very great irritation."† The following are among the occasional determining and predisposing causes. Injuries, as those inflicted during parturition; simple chronic ulceration; the cicatrices of dysenteric or tubercular ulcers; fistulæ and piles. "Of twenty-four cases in which inquiries were made as to cause, there was a history of previous injury in two, from rough riding in one, and from rough driving in one. Of twenty-four cases there was a

* Hulke: *Medical Times and Gazette*, 1873, vol. i. p. 407.

† Jessett: *Cancer of the Mouth, Tongue, and Alimentary Tract*.

history of previous disease of the part in seven, hæmorrhoids in six cases, fistula *in ano* in one case. In the last case the disease supervened in connection with the fistula, which was of forty-four years' duration." *

Age is, again, an unmistakable factor in cancer of the intestines. "Cancer of the intestines is very rare before the age of forty years; it is most frequent between the ages of fifty and sixty years." Isolated examples of rectal cancer have, however, been seen in young people. Mr. Allingham mentions cases coming within his own experience, and others have been seen by various observers. In these rare cases some exceptional cause is probably at work. It appears to me worthy of consideration here that pæderasty has been regarded as a cause of "fungus" of the rectum in females: "*ce mal est une suite du commerce infâme qu'ils ont en avec des hommes.*" †

Cancer of the rectum does not occur in the two sexes with any approach to that disproportion observed in cancer of the lips and tongue. "Of fifty-four cases, twenty-four were in males and twenty-seven in females." But on this point there is some difference among authorities. According to Mr. Allingham, "many more men are victims than women." Probably the difference in frequency in the two sexes is not extreme; and this would consist with the facts as to causation: the recognized influences will be nearly equally present in the lives of men and women.

In reference to the causes of epithelioma of the anus, which was met with four times in 123 cases of squamous epithelioma admitted to the University College Hospital, it is obvious that uncleanness, undue friction, and inflammatory states may readily occur at the anal aperture.

One of the most common of the innocent tumours of the

* Roger Williams: Middlesex Hospital Reports.

† Diornis: Cours d'Opérations, p. 398.

intestines is the mucous polypus. Like the malignant tumours, it is mostly seen in the large intestines, and especially in the rectum, and is often the sequelæ of catarrhal states.

These tumours, as with innocent tumours elsewhere, are associated with irritation of slighter degree and shorter duration than that in association with malignant growths. They also occur at earlier periods of life, and not seldom in children. (See p. 42, and cases 46 and 47 annexed.)

Cases Illustrative of the Facts Interpreted.

CASE 41.—*Encephaloid of Cæcum*.—"N. T., aged 12. Three weeks before admission fell from a height of six feet on to her back; she immediately complained of pain and difficulty in walking, and on the following day a swelling was, for the first time, noticed in the right inguinal region. Said to have always had good health; no history of any intestinal disorder.

"A healthy-looking, fairly nourished girl, with a very stupid aspect and manner. Walked with a limping gait, carrying the right side of the pelvis lower than the left. Autopsy twenty-six hours after death. Peritoneum was covered with puriform lymph; matting the coils of intestines together, surrounding the cæcum. The termination of the ilium was a mass of encephaloid cancer; its external surface was smooth, its shape oval, and size that of a small cocoa-nut. The mucous membrane of the cæcum presented a deep ragged ulcer leading into the mass." (*Medical Times and Gazette*, 1878, vol. 1, p. 279.)

(The etiological factors and their relations of sequence cannot be satisfactorily discriminated in this case. The notes are wanting in completeness and precision on certain points. The youth of the patient is of some interest.)

CASE 42.—*Cancer of the Cæcum*.—"D. E., married, aged 63 years. She stated that she had always enjoyed pretty fair health, but had never been very strong. She had had three children. About five years before admission she ruptured herself in the right groin through lifting a heavy weight, and had worn a truss from that time. Since then she had suffered from sickness more or less and

had to be careful about her diet. *Post-mortem*. A new growth involved the cæcum and part of the ascending colon, and was evidently of a cancerous nature. Its surfaces were irregular and sloughing; the ileo-cæcal valve seemed quite destroyed by it, and in that situation there was a ring of cancerous tissue which so encroached on the aperture that the tip of the little finger could hardly be passed through." (*Sieveking*.)

(The accident which happened to this patient was, not unlikely, the initiating cause of the cæcal cancer. Displacement of the intestines was followed by disturbance of their functions; probably by imperfect discharge of fæces from the cæcum with resulting irritation of the mucous membrane of the ileo-cæcal valve. These conditions conspired with others that were predisposing. The circumstances of the next case are very similar.)

CASE 43.—*Cancer of the Cæcum. Abscess in the Groin*.—"W. J., æt. 56, by trade a coach trimmer, of very temperate habits, had enjoyed excellent health till he ruptured himself by carrying a heavy weight; he afterwards had an abscess in the right groin. In October, 1855, he experienced pain and sense of heat at the lower part of the abdomen, and then found a swelling about the size of a walnut, which gave him great pain on pressure or on walking. The swelling enlarged day by day, but became less painful; and night sweats came on. On inspection there was an old inguinal sac on the right side quite free and empty. . . . On removing the cæcum and intestine, it was found that the posterior wall of the cæcum was destroyed by carcinomatous ulceration and offensive fæcal matter was poured out from beneath the iliac fascia, and the abscess extended downwards to the opening on the thigh. There was also an irregular nodulated growth extending from the mucous membrane of the cæcum, attached anteriorly near the valve, and surrounding the intestine." (*Habershon*.)

CASE 44.—*Cancerous ulcer of the Colon opening into the Duodenum*.—"Ann S., æt. 47, a greengrocer, who had worked hard, and drank freely. Five and a half years before admission she had free access to a fruit garden, and partook of fruit to excess; severe diarrhœa and depression followed. Eighteen months afterwards the skin

became slightly jaundiced, and her medical attendant found a tumour about the size of a hen's egg immediately above the spinous process of the ilium. She had also suffered from hæmorrhoids and tapeworm. On opening the colon *post-mortem*, there was found in the ascending part, just above the cæcum, a large carcinomatous ulcer, as large as the palm of the hand; it was circumscribed and surrounded by raised edges of morbid tissue." (*Habershon.*)

(This case is doubtless representative of numerous others where cancer of the colon is caused by excesses in eating and drinking. In the investigation of the causes of tumours of the intestines it is well to remember that the intestinal mucous membrane is an excretory surface for gaseous as well as liquid and solid matters. Inhaled impurities find a ready outlet through the intestinal canal and these when frequently present must now and then be injurious to the bowels, as we see in the slight purgation and subsequent atony of the colon which a pipe or cigar is able to produce in certain individuals.)

CASE 45.—*Cancer of the Rectum.*—"A farm-labourer, 63 years old. Until his present illness he had never been laid up one day. We found the anus quite healthy; not a trace of an external pile was visible. Passing the fore-finger into the gut, the mucous membrane, for the distance of about one inch and a half from the anus, was felt to be quite smooth, soft, and natural, and this part also retained its proper capacity; but beyond it the gut was almost blocked by firm solid knobs of tissue, jutting from its sides into the canal and so narrowing this that the finger-tip could only be just pressed into a small dimple between them, for a very short distance, and the upper limit of the obstruction could not be reached. He had never had any illness all life through until about one year ago, when he had an attack of diarrhœa, and he then, for the first time, noticed a little blood in his stools; later this was often repeated." (*Hulke.*)

(Accepting this as a typical instance of rectal cancer we see in it grounds for that rationale of the disease given at page 115. We fix attention upon the patient's age, upon the fact that the seat of the disease is at the terminus of the gut, where the wear and tear of functional exercise is at a maximum and where the

distance from the central source of nutritive supply is greatest, and we recognize in this conjunction of conditions the occasioning circumstance of that devitalization of tissue which the disease expresses according to our hypothesis. If cancer of the rectum thus depends on local exhaustion from local functional activity there is every reason to believe that this activity, passing natural bounds, is made possible by an exuberant constitutional vitality. Cancer of the tongue and lips showed us this with great clearness, and I venture to predict that men and women who suffer from rectal cancer will be found, generally, to have enjoyed for a length of time a large income in ingested aliment.)

CASE 46.—*Fibrous (?) polypus of the rectum.*—"W. S., aged 21, stated that he had been suffering from piles for over a year, for which he had been treated at a hospital, but had received no benefit. He complained that he had occasional bleeding after stool, which sometimes was pretty free. He also said that a bit of his body 'came down' at times, which he replaced by pressure from his finger. He suffered no pain, but had a sensation of discomfort in the part. On examination the anus appeared quite normal, but upon telling him to bear down, a slight ring of hæmorrhoids became visible, but no more than is frequently seen in a healthy rectum. Upon introducing the finger there was no pain, and the mucous membrane felt smooth and healthy and nothing abnormal could be distinguished. I was thus able to extrude the polypus from the rectum. The stalk upon which it was situated was quite three inches in length, having a uniform thickness of a No. 6 catheter. At the head of this was a soft polypus the size of a small walnut. The pedicle appeared to be attached to the lateral wall of the rectum, two and a half inches from the orifice." (*Cripps.*)

CASE 47.—*Disseminated polypi of the rectum followed by cancer of the sigmoid flexure.*—"A. C., aged 19. So far as was known, he was a healthy child until nine years of age. It was then noticed that, after being exposed to cold one day, he had considerable hæmorrhage from the rectum. Six months later a bleeding protrusion was occasionally observed after defecation. He was admitted into a hospital, and the protrusion removed when he was eleven years

old. The symptoms were temporarily relieved, but returned again in a couple of years. He was again subjected to operation, with only slight relief. Since that time he has on three occasions, at St. Bartholomew's and other hospitals, had growths removed from the rectum but without permanent benefit. When admitted in St. Bartholomew's he was extremely anæmic, having suffered severely from hæmorrhage for some months. . . . On examination under chloroform with the sphincter dilated, several mulberry-like growths were observed, varying in size from a pea to a filbert. Some of these had little or no pedicle, while others had well-marked stalks half an inch in length. By the aid of a duck-bill speculum, from twenty to thirty distinct polypoid growths could be seen; besides which, others could be felt higher up the bowel by the finger, which failed to define any limit to the diseased condition of the bowel." After several re-admissions "he was brought in in a moribund condition, his friends stating that since his last discharge from the hospital he had suffered dull, aching pain in the abdomen; that two days since he was seized with violent cramping pain in the lower abdomen, and sickness. On examination, he was found to be moribund, with the signs of peritonitis, and he died next day. On *post-mortem* examination, he was found to be suffering from adenoid cancer of the lower part of the sigmoid flexure, and there was at this point an almost impervious stricture of the bowel. The rectum below this contained a large number of polypoid growths similar to those that had been removed during the patient's lifetime; above the seat of cancer there were but few to be found, and in the ascending and transverse colon not more than three or four, and these were small and rudimentary. On examination the polypi proved to be well-marked examples of the adenoid variety. The large intestine above the stricture was enormously distended by fæces."* (*T. Smith: St. Bartholomew's Hospital Reports*, vol. xxiii. p. 229.)

(These two cases will supply the text of some important considerations. Though it is possible, and even probable, that in the case of the disseminated growths the disease was congenital, we note that both the patients were young, the fact being in harmony with the induction (p. 42) that benign

* See Cripps: *Diseases of the Rectum and Anus*, 2nd ed., p. 398.

growths usually appear at an earlier age than malignant ones. Then we observe that the polypi are not fused with the tissues like cancer of the rectum, but are thrust out upon the exterior of the body—a fact which bears witness to the superior tissue-resistance which goes with superior development and the strength of youth (p. 43). In connection with this it is interesting to read that the polypus appears to commence “as an hypertrophy of a limited portion of submucous tissue. The hypertrophied nodule is at first merely embedded in the rectal wall, but as it grows it becomes gradually extended into the canal of the bowel, so that after a while a pedunculated tumour is produced, still covered by mucous membrane.” (*Cripps.*)

The second of these cases demonstrates the fact that structures which are the products of histogenic dissolution (tumours) themselves undergo this process; but the second generation of germs so produced remain undeveloped—are cancerous. The malignant neoplasm succeeding the benign neoplasm supervenes upon increased age, upon long-continued irritation, and upon the intrinsic instability of a neoplastic structure. The following remarks of Mr. Smith will assure the reader of the actual conversion of the polypi into carcinoma, and there can be little question that undue actions in the sigmoid flexure, with resulting cancer at this point, were consequent on interference with the functions of the rectum which the masses of polypi occasioned:—“The microscopic examination of the cancer in this patient proved it to be similar in structure to the polypi, or as Mr. Bowlby describes it, ‘a typical cylindrical-celled adenoid cancer,’ while the bulbous ends of the polypi were, in the arrangement of their structures, like masses of adenoid cancer turned inside out. Mr. Bowlby informs me that in a vertical section of the cancer it could be demonstrated that the stalks of some of the polypi could be traced through the mucous membrane into the submucous structures, when they were continuous with the structure of the cancer.” Ocular proof of the changes is afforded by the drawing accompanying Mr. Smith’s paper.)

§ 25. *Recapitulation and Conclusion.*

After the commentations that have been made upon cases, it will not be necessary to epitomize the results of the present chapter at any length. In further evidence of those general conditions of tumour-disease considered in the chapter preceding, there have been brought forward fresh facts in connection with the more common tumours of each division of the alimentary canal; but more than this is the exposition of factors of an entirely different order. We have seen how, by a narrow scrutiny of the forces that play upon each distinct part primarily affected with the disease, there may be discriminated conditions that are causes in the practical sense of the word. The influence of these conditions, though co-operative with the conditions previously considered, is ascertained to be so predominant in the majority of cases as to constitute them the essential and indispensable factors—those factors in the absence of which the disease would be absent. Thus, whereas in Chapter III. it was impossible, at that stage, to estimate the efficiency, in tumour-genesis, of age and special and general nutrition, we are now in a position to do so approximately in most of the cases that have come before us, and we are forced to recognize the great efficiency of all those conditions that may be brought under the heads of “irritations” and “functional excitations.”

As bearing on the validity of our hypothesis, it should be noted how the recognition of such causes of tumours makes definitely intelligible a host of collateral facts. It were obtuse in one not to be impressed by the power of the hypothesis in effecting agreement among so many, varied, and hitherto confusing data. And the assumed *method* by which local irritation and local functional excitation exert their influence is of great probative weight. Whatever the nature of the actions distinguished as the causes of tumours in the alimentary canal, they may all conceivably induce the process of histogenic dissolution.

If we are to accept these results, we must not omit to deduce another result of great importance, namely, that the tumours of the special parts of the alimentary canal have each their special causes; here a leading part is played by tobacco or alcohol, there by the quantity and quality of the food ingested, and elsewhere by still other conditions. And in tumours of the same parts or organs there is never among the causes more than a resemblance—never complete identity in kind or in combination—but often considerable difference in both these respects. In this disease as in other diseases every case is truly a *case*. Finally, a distinctive etiological feature is the multiplicity of causes in most cases. Age, and locality in the anatomical sense, are almost ever-present influences in cancer, and these frequently work to one end in association with several other influences.

CHAPTER V.

THE SPECIAL CONDITIONS OF TUMOUR-DISEASE *continued*.

Cancer of the Breast—Adeno-sarcoma and the Benign tumours of the Breast—Cancer of the Uterus—Myoma and Sarcoma of the Uterus—Tumours of the Vagina and Ovary—Tumours of the Scrotum and Testicle—Tumours of the Penis—Recapitulation and Conclusion.

§ 26. *Cancer of the Breast.*

We may now deal with the tumours of the sexual system in reference to their known causes. From the great prevalence of cancer of the breast and uterus, tumours of the sexual system they take priority in practical importance over any other group of neoplasms. If we begin with the mammary gland it will be convenient to leave its benign growths until we have dealt with the carcinomata, and we may first place the facts in order and afterwards seek to understand them. It will not be advisable to dwell long upon statistical results, but rather to turn our attention as soon as possible to the study of concrete cases. By so doing we shall avoid some of the inevitable fallacies of statistical evidence, and bring ourselves into converse with most valuable facts of a kind beyond the practical reach of statistics.

The age-conditions of mammary cancer deserve to be very carefully noted. Of 194 cases*—

* Fink: Prager Zeitschrift für Heilkunde, B. ix. Hft. 6.

1 appeared between 20 and 25 years.					
3	„	„	26	„	30 „
7	„	„	31	„	35 „
17	„	„	36	„	40 „
29	„	„	41	„	45 „
29	„	„	46	„	50 „
34	„	„	51	„	55 „
35	„	„	56	„	60 „
18	„	„	61	„	65 „
16	„	„	66	„	70 „
3	„	„	71	„	75 „
1	„	„	76	„	80 „
1	„	„	80	„	85 „

An analysis of 1622 cases yields results in the closest correspondence. "The carcinomatous tumours develop, on an average, at the forty-eighth year; 81·20 per cent. appear after the age of forty; and they are never met with before the twentieth year."* Two or three apparently undoubted cases in young girls have, however, been reported.

Concerning the influence of marriage, among 236 cases observed by Billroth, twenty-three of the patients were single and 213 married.† Again, "of 600 women who had carcinoma, 80 per cent. had been or were married; 20 per cent. were single."‡ And the observations of others are fairly in agreement.

The fecundity of patients was noticed by Mr. Bryant in 485 women who had been married, and of these 360 were prolific, or 74 per cent., and 125 sterile, or 26 per cent.§ It is also said of these cases that "a large proportion of the prolific women were so to an extreme degree—ten or more children to one mother being a common note to find recorded . . . The breasts of married women and of those in whom the gland has

* Gross: American System of Gynæcology.

† Handbuch der Frauenkrankheiten, B. iii. p. 129.

‡ Bryant: Diseases of the Breast, p. 149.

§ Op. cit. p. 150.

been most active, are apparently more liable to cancer when the period of gland activity has passed than are the breasts of single women; a gland that has been functionally active being more prone in its period of obsolescence to become the seat of carcinoma than another which has never been called into activity." This very important induction the researches of others completely endorse. Of the 194 cases observed by Dr. Fink 168 patients were married, 21 were single, and in 5 the civil state was not declared. The following table of cases shows the relationship between the number of patients and the number of children they had borne:—

Children	0	1	2	3	4	5	6	7 and above.	Unknown.
	—	—	—	—	—	—	—	—	—
Patients	5	15	22	23	18	12	12	38	23
									Total 168

These results are substantially confirmed by the tables of Oldekop and Winiwarter, though that of the former gives a larger proportion of cases among sterile women.

Children .	0	1	2	3	4	5	More than 6.	Unknown.
	—	—	—	—	—	—	—	—
Patients .	19	11	12	16	12	10	21	11
								Total 122*

The etiological importance of fecundity is apparently sustained by the frequency with which the patients had nursed their children. Of Dr. Fink's cases 71·1 per cent. had borne children and 62·8 per cent. had suckled them, and Dr. Fink is moved by the facts to remark, "Nach diesen Resultaten ist es warhscheinlich, dass de wiederholte und oft lange Zeit andauernde Inanspruchnahme der secretorischen Thätigkeit bedingte Veränderung derselben von Einfluss auf die Entwicklung des Mammacarcinoms sind." The following table† gives more particularly the number of patients and the number of children

* Oldekop: Arch. f. Klin. Chir. B. 24, p. 537.

† Oldekop: Loc. cit.

suckled by each. It will be noticed that a considerable proportion nursed six and more children :—

Children suckled	0	1	2	3	4	5	6	More than 6.	Unknown.
Patients . . .	15	5	9	10	3	2	3	11	3
									Total 61

If the married state, child-bearing, and lactation may be concerned in the genesis of mammary carcinoma, it seems only consistent to take note of the menstrual function. The testimony on this point shows that menstruation is seldom disturbed, and in the majority of cases the function persists up to the onset of the disease.

Statistics establish the fact that the right and left breasts are nearly equally liable. "In three hundred, or half of the six hundred cases, the right gland was the seat of disease; in 272 the left; and in twenty-eight both glands were involved."* The cases tabulated by Dr. Fink, show that the disease attacked the right breast in ninety-five and the left in ninety-nine instances.

As to the part of the breast most frequently first affected the results of observers are conflicting. According to Dr. Fink in a considerable majority of cases the disease begins in the upper and outer quadrant. Dr. Gross writes as follows :† "While Oldekop and Winiwarter agree that the upper portion of the outer hemisphere of the mamma is its most common seat, my own one hundred cases show that fifty-six occupied the vicinity of the nipple, seven having been discovered immediately behind that body, nineteen at its outer side, twelve at its inner side, six below and twelve above. . . . Of the remaining forty-four cases, thirty-three were located towards the outer circumference and eleven toward the inner periphery, and of these only eighteen occupied the upper hemisphere. On the whole, the seats of the election of cancer are the upper and

* Bryant: *Op. cit.* p. 150.

† Tumours of the Mammary Gland.

outer quadrant and the immediate neighbourhood of the nipple." These conclusions I think we may accept, and for reasons that will presently appear.

Not a few cases are associated with injury to the breasts, either injury from mastitis (inflammation) or traumatism. "That injuries, such as contusions and blows, are efficient causes of carcinoma, cannot be doubted. Thus the affection was ascribed to trauma in 202 or 13·36 per cent. of 1511 cases." (*Gross*.) Mr. Ericson* expresses himself as follows:— "The number of instances that have fallen under my observation, in which a squeeze of the breast has speedily been followed by the appearance of a cancerous tumour in it, leaves no doubt whatever in my mind of the truth of the popular belief that associates the injury with the disease, in the relation of cause and effect."

In reading the reports of cases the concurrence of mastitis and cancer in the same breast is strikingly frequent. "Out of 360 cases of women who had borne children, mastitis had occurred at some antecedent period in eighty.† Oldekop met with a history of early mastitis in thirty-six of his patients and in twenty-two of these cancer supervened later in the same breast, while in eleven the later history was wanting, and in three the opposite breast was attacked.

Does the general health of patients who suffer from mammary cancer supply any etiological indications? On this point we have the testimony of Mr. Bryant "that there are few patients admitted into metropolitan hospitals with a more general healthy aspect than those who have cancer of the breast. At least half the cases who have this disease present the appearance of perfect health. Two-thirds of the remainder look as healthy as the bulk of those who are doing the work of life well. Whilst in the sixth, not included in either of these classes, some general evidence of illness may be made out; the general evidence depending more upon mental anxiety and

* System of Surgery.

† Bryant: Op. cit. p. 161.

apprehension than any real influence of the disease upon the functions of the body." With these statements the numerical data of Dr. Gross are in full accord. "Out of 627 subjects in whom the point is noted, 417, or 66·50 per cent., were in excellent health; 129, or 20·57 per cent., were in indifferent or moderately good condition; 81, or 12·92 per cent., were broken down from the effects of the disease." Out of 170 cases in Winiwarter's tables 58 were in good general health, 21 were well and tolerably nourished, 16 were thin and pale, and 9 were ill-nourished and cachectic.*

Numerous and important conditions, over and above those now set down, enter into the etiology of mammary cancer. But they cannot suitably be included in this general survey, and we must take them up in the interpretation, to which we may now address ourselves.

How must we construe the facts by which we are confronted? It seems to me that an explanation of this disease must rest on our hypothesis. First let it be firmly grasped that mammary carcinoma of every variety originates in the parenchymatous elements of the gland. It has been shown by pathologists to the entire satisfaction of the inquirer that the working cells of the breast are those really involved. Objective evidence, too, has been presented (§ 7) demonstrating that the primary changes in these cells—the changes concerned in the *genesis* of cancer—are those comprehended by the term histogenic dissolution. Now histogenic dissolution as a biological fact signifies to us that the protoplasmic energies of the cellular units have been unduly drawn upon in meeting incident forces—in the performance of function, in adjustments to the circumstances of existence. Let us now see whether the known conditions of mammary cancer answer to this generalization.

* Beiträge zur Statistik der Carcinome. (See also Paget: Surgical Pathology, p. 635.)

It is needless to dilate upon the facts as to age. Cancer of the mamma seldom or never appears before the twentieth year, and in a large majority is met with after the age of forty. Next, significantly enough, all the foregoing data apply to the mammary glands of *women*. Breast-cancer in the male, which we shall presently consider, is not unknown, but the proportion given by Mr. W. Roger Williams in his well-known statistical reports is only one case in the male to 102 in the female. This fact alone is sufficient to assure us that cancer of the mamma is in some close relation with the functional activity of the female organ. If the disease were independent of the difference in the life-histories of male and female glands there should be no such difference as there is in the frequency of the affection in the two sexes. But pointing most plainly in this direction are the figures which show the relations to the functional life of the mammary gland. Analysis of the large number of cases collected by Dr. Gross proves that in 18·80 per cent. the disease was coincident with the period of most active function; in 81·20 per cent. the disease began after the age of forty, or during the period of declining function; and in not one was the disease observed during the period of developing function. Here are the very conditions of histogenic dissolution; in a large majority of cases the disease appears during the period of the natural obsolescence of the gland. The observations of Sir James Paget and Mr. Bryant lead to identical conclusions, and it has been emphasized by Dr. Creighton that "*scirrhus tumour of the breast is a disease of the obsolete breast, or of the breast becoming obsolete*;"* and Gross says, "It is certain that cancer is a disease of the obsolete or obsolescent breast."† Now obsolescence of the breast is accompanied by a gradual disorganization (dissolution) of its secreting mechanism. (*Creighton.*)

Eighty per cent. of the women affected are married women. In the face of the Registrar-General's return of the proportion

* Physiology and Pathology of the Breast. † American System of Gynæcology.

of married and single women in the general population this cannot justly be regarded as evidence of the same tenour. In London 84 per cent. of women over thirty-five years of age are or have been married. All we can say is that the evidence as to the influence of marriage is not contrary and may possibly be affirmative.

But affirmative in a high degree is the observation of Mr. Bryant and others that women who have had many children are exceptionally prone to suffer from mammary cancer. Making allowance for possible qualifying considerations, it must, I think, be granted from the facts adduced that excessive fertility is a factor of considerable moment. And from the table of Oldekop we may gather that suckling has a perceptible influence. Thus, the actions which above all others tend to deplete the mamma of its contained energies are proved to be decidedly instrumental in the production of cancer in its substance.

It was found that the right and left breasts are nearly equally liable and, consistently, they are nearly equally subject to the demands of function. There are, however, slight though distinct differences in statistics as to the side most frequently affected, and perhaps these differences depend in part on the social position of patients. On the whole, I am inclined to think that the left breast is rather the more liable. Right-handedness among working women might be expected to lead to a slightly greater use of the left breast. The left breast in women is almost invariably larger as if from greater use. Out of 151 hospital cases 67 were of the right breast and 84 of the left.*

Out of 100 cases observed by Dr. Gross the disease occupied the vicinity of the nipple in 56. If the disease is related to child-bearing this fact may be at once explained. Those acini and lobules nearest to the nipple will be called upon for greater functional service than acini and lobules at a distance, and we

* Middlesex Hospital Reports.

might anticipate as a consequence their more frequent cancerous dissolution. That the new formation does, in a large proportion of cases, start from structures near the mamilla is certain. Dr. Gross's observations are borne out by the frequency with which the nipple is retracted in mammary cancer at an early stage. This retraction is a common symptom, but cannot occur where the disease is limited to the periphery of the gland.

There is also a variety of carcinoma that takes origin in the gland ducts: structures easily subjected to undue functional exercise and to irritation.

But what must be said of the beginning of the disease in very many cases at the upper and outer periphery? Two tenable suggestions may be thrown out. The commencement of the disease at this situation may be connected with the pressure of the suckling infant's face and the gentle butts to stimulate the excretion of milk which children at the breast are wont to make. The distribution of such stimuli will be mainly confined to the upper and outer quadrant. Or, possibly, the disease, beginning here, grows from the imperfectly developed gland-like structures described by Dr. Champneys as axillary lumps or milk-producing sebaceous follicles.

If, as the facts so plainly assert, functional stimulation of the breasts does predispose them to cancerous decay, it is a consonant circumstance that there is rarely noted any irregularity in the performance of the menstrual function. This testifies to sexual vigour, and the fact finds its correlative in the good general health of patients. As we saw in cancer of the alimentary tract, constitutional strength will make possible those local functional activities which lay the foundation of the disease. Regularity of the periodic excitations of the breasts in menstruation, the strength to bear children and to suckle them, are physical impossibilities without a certain stamina and fair nutrition. Hence we see the import of the fact expressed by Mr. Bryant, "that there are few patients admitted into metropolitan hospitals with a more general healthy aspect than those who have cancer of the breast." But from considerations

already pointed out, we shall not be inclined to withhold assent to the opinion of many that untoward conditions affecting the entire system will occasionally be decided influences both in the genesis and progress of the disease (see p. 110). They will be so, the ground having been prepared by locally incident conditions. On this matter we read as follows :—"The statement may certainly be made, without fear of contradiction, that all circumstances tending to depress the vital powers are very commonly associated with the development of cancer. Thus severe mental distress, losses of blood, poverty, intemperance, are commonly marked features in the lives of individuals afflicted with this disease."* "Mental anxiety as a cause of carcinoma must not be omitted, although to adduce proof of the truth of the proposition may be difficult; to say that it is an antecedent of many cases of carcinoma is, however, a fact which the experience of most surgeons would support."† "Of 38 breast cases 24 patients gave a history of sorrow and anxiety, 4 of hard work, while one case was doubtful."‡

On this interpretation of cancer of the breast there exists a difficulty in the occurrence of the disease in married but sterile women, in single women, and in males. The proportion of the single and sterile women to the married and fertile is very small according to some observers, but considerable according to others. In only 23 of 236 cases were the patients single, if we accept the results of Prof. Billroth; and in only 5 out of 168 cases were the patients sterile, if we accept those of Dr. Fink. We find one case in the male to 102 in the female. Now, although in these cases there is no evidence of functional strain to point to, I think we may still suppose that the causes at work are like those in other cases. In individuals of the three classes under consideration, the mammary glands are not wholly absolved from functional action. In single women, at the menstrual period, the breasts are always stimulated, and in married but sterile women there are additional excitations from sexual

* Birkett: Holmes and Hulke's System of Surgery.

† Bryant: Op. cit. p. 169.

‡ Snow: *Lancet*, 1881, vol. ii.

cohabitation. The latter circumstance affects even the glands of some males, but in the least degree; a degree corresponding to the rarity of the affection in men. If it be remembered how the mammary glands show signs of activity at puberty in both sexes, and that this activity in boys as well as in girls may go on to the formation of an abscess, and that inflammation of the breast is by no means uncommon in virgins after menstruation, and in married childless women, if we remember these truths we shall see that occasional cases of cancer in young, unmarried, and sterile women, and in males, may yet be accounted for on the general theory. These causes, then, where other causes are exceptionally favourable, will suffice to prepare the elements of the structure for histogenic dissolution at the period of natural obsolescence. It favours this contention, that a determining cause, such as traumatic injury, is very commonly required for the genesis of cancer in the male breast (see appended cases). Mr. Roger Williams found a history of previous injury or disease in 53 per cent. It is also interesting that "the average age at which the disease originates in males is 2 years later than in females . . . a relatively large number of the male cases begin over 70"; the significance of this being, probably, that cancer of the male breast does not easily arise without the supplementary influence of senile decay. Furthermore, Mr. Williams has shown that in 14 cases where the seat of the initial lesion was noted, the disease began in the elements about the nipple. "In 8 the disease was central, being situated underneath the nipple; in 3 it was near the nipple; in 1 below the nipple and to its axillary side; in 1 below and to its sternal side; and in 1 above the nipple and to its axillary side."*

Thus far we have dealt with what may be regarded as the fundamental factors. In many cases these factors are in themselves efficient, but in many others—it is impossible to speak with numerical exactitude—they are merely predisposing. Injury and mastitis are frequently the determinants. And among influences of this order must be mentioned the effects of

* On Cancer of the Male Breast: *Lancet*, vol. xii., 1889, p. 262.

the corset. Here is an injurious condition in daily action. The constant pressure of the corset will necessarily affect the structure of the gland disastrously, especially when used to give prominence to the breast by thrusting the mamma upwards. It is known that depressed nipples and inflammation may ensue from wearing this instrument, and we shall presently see from the cases that these effects lead to cancer.

Acceptance being accorded to these views of mammary cancer, it may yet be asked why certain women are unable to bear without this grave consequence the apparently due discharge of a natural function? A deeper question remains unanswered, we desire to know the causes of the causes. It appears to me highly probable that mammary cancer is not without relations to a cardinal fact of our social organization. I refer to the institution of monogamic marriages. That monogamy as it exists with us is not a primitive form of sexual relationship, but an advanced and comparatively modern product of social evolution, is a quite sustainable proposition. With all the immense advantages which accrue to the family and the state from the marriage of one man with one woman, rather than of one man with two or more women, there is yet imposed thereby, upon the individual woman, greatly enlarged duties to the race. This may well be the reason why a *seemingly* normal amount of maternity is followed by cancerous decay of the breasts. Doubtless it is not simply the large number of children which each married woman on the average is required to contribute which conduces to the break-down of the sexual system, but this circumstance in co-operation with excessive demands upon her energies for purposes other than those of reproduction. We rarely see anywhere the intelligent fostering care which every married woman requires if she is to properly fulfil those great ends which Nature has designed her for. If well-circumstanced in life, false and perverse conceptions of her true functions in the economy of the social organism lead often to an expenditure of forces which entirely unfits her for the bearing and rearing of children. And lower in the

social scale it is usually the lot of women to perform the duties of motherhood under the worst possible conditions. Those who with good physiques are bearing many children, yet work like men, will be found, I feel sure, to furnish the largest number of cases of cancer. It is needful to remember that the sexual organs ministering to the life of the species, are, in the highest animals, accessory to those organs which minister to the life of the individual. In the lowest animals individuation is subordinate to reproduction: each creature lives less for itself than for the race; but as we ascend there is a gradual reversal of this relation. The subsidiary character and partial independence of the sexual system in ourselves is reflected in the fact that the sexual organs are not vital parts, but may be ablated without seriously deranging the more fundamental functions. Many are the ways in which the supremacy of the individual over the sexual life in man and animals is shown. It is shown whenever large draughts are made upon the energies in furtherance of individuation, as in severe manual and mental labour; it is shown in diseases where the expenditure of energy is at a maximum, and the income from lessened supplies at a minimum; under these circumstances there is an immediate diminution in the procreative appetite and powers: the available forces are drawn off from the accessory to the fundamental organs. Another instance is seen in the organismal changes induced by extreme changes in the external conditions. Animals that breed freely in England will become sterile for a time after transportation to Australia. Here the energies are used up in effecting new equilibrations, or adaptations to new conditions—processes of individuation—and the reproductive system is impoverished correspondingly. The climacteric in woman and man has the same meaning. As the total potential and active energy of the body declines with increasing age, the non-fundamental sexual system is called upon to yield up its stores of force and to cease making further demands upon the organism; the uterus, breast, and testicle atrophy, and sexual desire and capacity disappear. Now in proportion as the physiological expenditure, either for individuation or

reproduction, has been great, so will the climacteric come early and be strongly marked, other things being equal. We have seen how closely connected is cancer of the breast with the natural obsolescence of this organ, and how closely it is connected with those conditions which are likely to make the obsolescence complete and premature.

Cases Illustrative of the facts Interpreted.

CASE 48.—“Mrs. E. R. B., æt. 46. External appearance that of a singularly comely interesting woman. At the age of twenty-eight, when confined of her first child, she suffered from abscess in the right breast. This gave way of itself, and she was not prevented from continuing her suckling. She never had any blow or injury to the breast. About eighteen months since she noticed that the nipple of this breast was disappearing, and this circumstance was followed by a general hardness increasing gradually so as to involve the entire organ. After a time she became pregnant, and was delivered about five months since of a remarkably healthy child. Soon after her confinement the breast broke into a sore, and thenceforth it contracted in dimension. The right breast has entirely disappeared, its place being occupied by a deep cleft, situated beneath the pectoral muscle. There is no great sore at the bottom of this fissure, but only a few flattened granulations.” (*Pemberton.*)

(This case serves admirably to point the salient features of scirrhus cancer. First mark how truly the word “dissolution” expresses the essential nature of the disease. To the external vision the gland has “entirely disappeared,” and extending our vision in imagination to the inmost changes in the cells, we can readily conceive from the gross and coarse effects how the glandular elements first dissolved into swarms of germs and then the germs disappeared, in part, by absorption. The dissolution here is not an ulcerative disintegration. We mark also the indications of good physique in mother and child, and the origin of the disease at the very seat of a previous inflammation. Unfortunately we are not told how many children the patient bore and suckled, but it is a notable circumstance that the breast damaged by mastitis, the patient afterwards nursed

with. Here, perhaps, the disease was the summation of mastitis, and the gland's functional performances.)

CASE 49.—“A woman had a child at eighteen years of age. The child died when it was a month old, and her breasts were left to the disturbance which usually ensues in prematurely arrested lactation. At the age of thirty-four she received a blow on the right breast. This was followed by no manifest change of structure, but for some days by feelings of swelling and tension at the menstrual periods. At thirty-nine she received another blow upon the same breast which was followed by an increase of pain. Soon afterwards she was exposed to cold, and then there ensued erysipelatous inflammation of the breast followed by induration of the part of the mammary gland. This, however, continued without change for four years; but then, after menorrhagia a tumour appeared in the breast. When this was removed or partially removed, it was found to be not a cancerous, but a cystic tumour, with growths from the interior surfaces of the cysts. She remained well after this, the wound having perfectly healed, for twelve years more, and in this interval, she ceased to menstruate; but now, when she was fifty-five years old, after having a whitlow and inflamed lymphatics of the right arm, another tumour formed in the breast, which had every appearance of being cancerous. It was removed; but it recurred, and ended fatally.” (*Bruch, quoted by Sir James Paget.*)

(Here the chain of circumstances affords a clearer perception of the rôle played by age in the genesis of cancer. The cumulative influence of many superadded causes at last acquires effective volume with the advent of the degenerative changes incidental to advanced life. It is curious and instructive that this comment is almost a reproduction of that made by Sir James Paget. Though with a real difference of underlying conception the facts strive to speak for themselves. Referring to the local conditions he says: “They had existed, or had been reproduced from time to time, for a period of upwards of twenty years; yet being alone, they had been insufficient; and no cancer appeared till the time when, at a more favourable condition of age, the cancerous condition of the blood was

manifested, and filled up the measure of the necessary precedents of the disease.”

This case also exemplifies singularly well the fact that while the protoplasmic changes which lead to histogenic dissolution and the formation of a tumour are relatively superficial, the resultant effect is not a growth of low organization with a correlatively low resistance in the tissues, but a growth of high organization with correlatively high resistance.)

CASE 50.—“A healthy widow, aged 30, with one child ten years of age, consulted Mr. Birkett in October, 1859, for a small painless swelling, situated in the clavicular lobe of her left breast, which had been growing for seven months. . . . In December, 1859, the tumour was excised with some of the breast gland, and the patient recovered. . . . On section the tumour was formed of a cyst, which contained serum, and communicated with a duct near the nipple. . . . The patient remained well for eleven and a half years, when a carcinomatous tubercle appeared in the scar, which enlarged and ulcerated.” (*Bryant.*)

CASE 51.—“Eliza B., aged 62, the mother of three children, all of whom she suckled with the right, but not with the left breast, as it was not fully developed. During the second lactation an abscess appeared in the left breast. One year before she consulted me, she noticed a small lump in the left breast. . . . When seen, the left breast was infiltrated with some neoplasm.” (*Bryant.*)

CASE 52.—“Ann G., aged 46, the mother of twelve children, the youngest being one year old (she never suckled with her right breast, as the nipple was retracted), came under my care with acute carcinomatous infiltration of her right breast, with nodular skin tubercles over the gland, and enlargement of the axillary glands.” (*Bryant.*)

CASE 53.—“Mrs. S., aged 42, the mother of four children, the youngest being one and a half years, who had not nursed with her right breast from defect of the nipple, came to me when pregnant seven months, with her right breast infiltrated and nipple ulcerated.” (*Bryant.*)

CASE 54.—“Mrs. G., aged 45, the mother of one child, aged 17.

She had suckled with her right breast, but not with her left because she had no milk in it, and the nipple was retracted. For six years she had had a discharge of a clear fluid from the retracted nipple of the left breast, and which at the catamenial periods was increased; the fluid at times was like 'treacle water.' Three months ago this flow stopped and a lump appeared—cystic duct sarcoma." (*Bryant.*)

(The cases here clustered may be pressed to impart invaluable instruction. What antecedent circumstance caused retraction of the nipple in these patients? Almost certainly the use of the corset. If so it is made manifest that the disorganization—sometimes ending in abscess—induced in this way may be a factor of considerable power. It is stated that half the cases of mammary abscess in puerperal women are associated with defective nipples. (*Birkett.*)

CASE 55.—*Cancer attributed to the pressure of the corset.*—"S. T., æt. 43, married, a delicate-looking woman, came, January, 1862, on account of a tumour in the left breast. About two years since she first noticed a small painful swelling in the substance of the left breast, produced, as she thought, by the pressure of the steel in her stays. From the commencement she had acute lancinating pain, which occasionally extended down the arm. The breast is charged with an uniform hard tumour, it is already contracted in size, and immovable on the pectoral muscle beneath. The nipple is retracted. The left breast is small but unchanged. May 11th, 1863.—I again carefully examined Mrs. T., not having seen her for many months. She informs me that about nine months since she observed hardness in the right breast, commencing about the nipple, which gradually disappeared. The left breast is entirely gone." (*Pemberton.*)

CASE 56.—*Cancer following a blow.*—"M. R., a healthy-looking old woman, aged 72. She was a married woman, and had had eight children, all of whom she had suckled without trouble. She had always enjoyed good health. Five years ago she struck her breast severely against the corner of a washing tub; swelling and pain followed, and when the immediate effects of the injury had subsided, a lump remained. Six months ago this lump suddenly began to enlarge and became the seat of pain." (*Bryant.*)

(The facts of this case permit us to say with some confidence that child-bearing, lactation, and injury, together constituted the pathogenic conditions.)

CASE 57.—*Acute scirrhus following a blow in an unmarried woman.*—“Miss V., æt. 32, fresh-coloured, and very healthy looking, was brought to me on account of a tumour in the left breast. Ten months since a large sugar cone fell against her chest, and bruised the gland, so much so as to cause pain. She forgot this circumstance until four months since, when she detected a hard substance in the breast, and noticed that the nipple had disappeared. Up to this time there was no pain, but she had become thinner.” (*Pemberton.*)

(One of the implications of the present case, if we place it in apposition with the preceding, is that the effective value of like causes differs greatly in different organisms. Much more importance must be attached to injury followed by cancer in a young, unmarried, healthy woman than to injury in an old woman who had borne and nursed many children.)

CASE 58.—*Acute brawny carcinomatous infiltration of breast and skin over it; death in six months.*—“Ann R., aged 53, a married woman, the mother of eleven children, the youngest being twelve. She had been perfectly well up to three months before, when she noticed a swelling in her breast, which rapidly increased and complicated with pain down to the right arm, and swelling. Within six months of the first appearance of her trouble she died with internal cancer from exhaustion.” (*Bryant.*)

CASE 59.—*Carcinoma of the right breast, following (? associated with) eczema of the nipple; excision of tumour, which was a typical duct cancer; cure.*—“J. G., aged 53, a healthy woman, the mother of several children, all of whom she suckled without difficulty, came under my care with a tumour in her right breast. It gave no pain, and she disregarded it. In August, 1885, the nipple became sore, and she sought advice. Some application was applied to the nipple, and the eczema improved, but never got well. The lump in the breast during this time had much increased. When admitted under my care into Guy’s Hospital there was a patch of

eczema, about the size of a florin, occupying the site of the right nipple, which had become obliterated. Behind and to the outer side of the eczematous patch there was a hard nodular tumour measuring three inches transversely and about two inches vertically, in the substance of the breast. Mr. Targett, the surgical registrar and pathologist, examined the tumour, and gave the following report:—‘The microscopic examination showed the changes of chronic eczema in the nipple and areola. There was proliferation of the epithelium along some of the ducts, and especially in the terminal acini. In the latter situation there was much small cell infiltration around groups of acini, and in this manner they were converted into the alveoli of fully developed carcinoma.’” (*Bryant.*)

(These cases illustrate the relation of cancer of the breast to fecundity and lactation. The second of them is quoted at length in support of the opinion that eczema of the nipple, to which Sir James Paget has drawn attention, is not a cause of cancer, but an effect or accompaniment of cancer already established in the lactiferous ducts. This, the researches of Dr. Thin and others have demonstrated.)

CASE 60.—*Scirrhus associated with Encephaloid tumour of the breast.*—“A. S., æt. 36, a married woman, sent to me on account of disease in the left breast. In August, 1856, one month after her confinement, she suffered from milk abscess. This left a hardness in the breast, above the nipple. In December, 1857, three months after the birth of the second child, and whilst suckling, the hardness grew into a tumour. Subsequently, fluctuation appearing to be present, an opening was made and a glairy fluid like that contained in a cyst was let out. The breast is very large, very hard, and gives no trace of natural structure, with the exception of the nipple and the integuments below, which are entirely unchanged. Above the nipple the disease has burst outwardly, and has pushed forward a fungus-looking growth. Examination of the tumour:—The lower part presented the well-marked characters of scirrhus cancer, whilst the upper terminating in the fungous protrusion was of the encephaloid variety.” (*Pemberton.*)

(Again, as in so many cases, cancer is sequent here to injury

done by inflammation. It is to be noted also that the growth of the tumour received an impetus from the nutritial activity attendant upon activity of function. The structural characters of encephaloid cancer are due, as we have learnt, to the extreme simplicity and reproductive activity of the neoplastic elements, and there is hardly any doubt, I think, that the encephaloid growth in the present example was instigated by the incision into the tumour. The effect of this would be to further depress the vitality of the structure with an extension of the process of histogenic dissolution and a reduction in the developmental power of the cellular product. There are many facts to bear witness to the truth of the following remarks by Mr. Pemberton:—"The progress of these cases is often very materially hastened by incisions or punctures which have been rashly made into the tumour on the supposition that they were abscesses or other collections of fluids. Fungus growths, which bleed profusely, protrude from the incision or puncture.")

CASE 61.—*Cancer of the breast during pregnancy.*—"A woman, aged 40, of very healthy and cheerful appearance, already the mother of eight children, was confined with a ninth five months ago. About twelve months prior to this ninth confinement, her attention was drawn to a small lump in the substance of the right breast. She took no notice of it whatever, thinking she had 'caught cold.' For a period of seven months it caused her no uneasiness and gave her no trouble whatever, and did not increase. During this time she became pregnant, and, at the fourth month of the pregnancy, the tumour in the breast began to enlarge and give her very intense neuralgic pains. In the last months of pregnancy the tumour rapidly increased in size, and she suffered more or less pain, and about a fortnight before her confinement the skin gave way and an ulcer was the result." (*Goulden : B. M. J.* 1878, vol. xi. p. 560.)

CASE 62.—*Amputation of the breast of a pregnant woman for carcinomatous disease.*—"The patient was in the sixth month of utero-gestation. She had a cancer of the breast which was rapidly growing, painful, and causing much inconvenience and discomfort. The operation was attended with some amount of hæmorrhage,

explained by the fact that the cancer was fed by a large number of vessels, and the gland generally was much congested, as a necessary accompaniment of the pregnancy." (*Savory : Lancet*, 1863, vol. ii. p. 365.)

(Case number 61 is probably an instance of cancer caused by excessive exercise of the mamma—that is, by its exhaustion—and of growth promoted by exercise. Case number 62 supplies direct evidence of the increased vascularity of a breast-tumour in pregnancy. Already at § 19 we have considered the dependence of tumour-growth upon nutritive supply.)

CASE 63.—*Acute cancer of both breasts and ovaries in a woman aged 24.*—"E.W., æt. 24, a rather stout good-looking Irish brunette, was admitted April, 1875, having then in her right breast, mostly lying in its sternal half, a very hard subglobular mass, about three inches in diameter, with an ill-defined border and slight adhesion of the skin at its most prominent part. Between this mass and the sternum were two scars of an abscess, which seven years ago followed her first and only confinement. The nipple was flat; she said it had always been so, and that owing to this she had not nursed with this breast. She menstruated regularly, and her appearance was that of a person in vigorous health. None of her relations had, to her knowledge, had tumours of any sort In November a sudden and rapid evolution of secondary knots took place, beginning in the right mammary region; next the left breast became, as it were, infiltrated with a diffuse scirrhus growth, which quickly made it a large, hard, stiff, hemispherical mass. Simultaneously with this, there was a rapid dissemination of scirrhus knots through all the soft tissues over the front and sides of the chest, converting them into an inflexible brawny cuirass. In less than a fortnight from the beginning of this outburst her chest had become quite fixed. She was now unable to lie down; her dyspnœa was terrible to witness. She was quite cyanosed and died suffocated." At the *post-mortem* examination, "the extremely well-nourished condition of the body was noticed. A thick layer of healthy looking fat occurred in the abdominal parietes, and the omentum was laden with fat. . . . There was no peritoneal cancer, nor were any of the lymphatic glands within the abdominal cavity affected; none were even enlarged. The liver, spleen, and kidneys

were natural. In the pelvis, however, it was found that the cancer had attacked the ovaries symmetrically, and so symmetrically, that in size and appearance these organs differed hardly at all from each other. Each was enlarged to the size of a chestnut, was adherent to its Fallopian tube, and presented slight lobulation. On section the ovary was soft, of a pure white colour throughout, presenting no traces of normal structure. Microscopically, it presented the characters of a medullary cancer, the stroma being reduced to a minimum." (*Cayley: Trans. Path. Society Lond.* v. xxvii.)

(The interest of this case concentrates round the question whether the disease of the left breast and ovaries was primary or metastatic. The weight of evidence, it seems to me, favours the former alternative. Although the patient was exceptionally young, probably some congenital weakness of the sexual system caused the ovaries as well as the mamma to succumb to the strain that had been put upon them. Of the extent of this strain we are ignorant; it is, however, in evidence that the patient married and bore a child at a very early age—17. The early inflammation of the right breast determined the commencement of the disease on that side, and the terribly swift advance of the malady may be ascribed to the highly-nourished state of the tissues.)

CASE 64.—*Cancer of the breast following sorrow.*—"A lady aged 40, wife of a gentleman in comfortable circumstances, strong and previously healthy, leading an easy life with no family, having a cheerful disposition, without family history of cancer, and never having sustained an injury, became greatly affected at the death of her brother after a short illness, and allowed this to prey on her spirits for some time afterwards. Within a few weeks a small lump appeared in her left breast; she paid no attention to it till six months afterwards, when, on examination, there was found a well-marked scirrhous tumour, with enlarged axillary glands." (*Snow.*)

CASE 65.—*Cancer of the Male breast.*—"E. R., police constable, while arresting a prisoner, received a kick on the left breast; it was not very severe but caused him some pain at the time, and did not prevent his being on duty the following day. Twenty-four hours after the injury there was a bruise the size of a florin around

the nipple. The marks of this remained for some weeks and then disappeared. Ten weeks afterwards he noticed for the first time some hardness round the nipple, about the size of a small marble. He treated this by fomentations and poultices, but it continued steadily to increase. On entering the hospital, rather more than a year after first noticing the growth, there was a large projecting tumour, the size of a foetal head; the skin over it was dusky in colour and firmly adherent, while in the axilla were two large glands the size of walnuts. He was a strong burly man, no family history of cancer, and had got rather stouter than thinner during the last six months, since he had been off duty. The tumour was malignant." (*Cripps.*)

CASE 66.—*Scirrhus affecting both breasts in a Male.*—"Patient was 61 years of age, of active and steady habits, and apparently in perfectly good health. About eighteen months before I saw him he noticed a lump in the left breast, but it did not pain him until six months ago, when it became uncomfortable from occasional pricking and shooting pains. About three months ago he also noticed a small lump in the right breast, but this had not been painful. There was no history of tumour or cancer in the family. At the time when first seen, March 13th, 1874, the left breast showed a tumour involving the skin to a limited extent below and outside the nipple. Its surface was covered with thinned, red, adherent skin; its substance was of scirrhus hardness, somewhat nodulated towards the nipple, which was slightly retracted. There was no discharge from the nipple. In the right breast a small hard mass could be felt, situated just underneath the nipple, but it was not well defined and it did not involve the skin." After removal of both breasts, the scirrhus nature of the tumour was proved by microscopical examination. (*Wagstaffe: Tr. Path. Soc. Lond. v. xxvii. p. 239.*)

(The second of these cases (No. 66) tends to confirm the induction that the *fundamental* cause of cancer of the male breast is that of the same disease in the female—periodic stimulation of parts in sympathetic connection with the organs of generation; for the bi-lateralness of the disease and the attendant circumstances oblige us to recognize a cause operating upon the sexual system as a whole. So that in the first case (E. R.) the resulting neoplasm was due to the inferior viability of the

particular tissues injured *plus* the injury. It may be inferred that if this patient had been kicked on the arm instead of on the breast, cancer would not have been the sequel.)

§ 27. *Adeno-sarcoma and the Benign Tumours of the Breast.*

The mammary neoplasms whose conditions we have yet to consider are the sarcomatous, cystic, and benign growths.

Sarcoma of the breast is usually adeno-sarcoma, and contains varying amounts of structural elements derived from both the parenchyma of the organ and its connective tissue frame-work. Tumours of this kind may without impropriety be classed with the cancers. They "rarely attack the breasts of young women, but rather those over 30 or 35, and they are not uncommon in women about 50 years of age."* They are also, perhaps, most frequently met with in married and prolific women, and may be caused by injury and mastitis.

If we suppose these growths to originate like the cancers in the want of viability in certain cellular units, the dissolution by histogenesis must be extended to the connective tissue of the mamma as well as to its glandular elements. It is reasonable to assume that in some persons the conditions which induce partial dissolution of the parenchyma will concomitantly induce the same in the connective substance. Though in the majority of cases the agencies which rob the tissues of their vitality will affect the proper working cells of the gland and set up cancer, yet the supporting (connective) structure cannot remain unaffected. In different degrees the influence of such agencies must be felt by every constituent of the organ.

The most interesting facts to us in connection with cystic disease of the breast are that it is a degeneration of old glands, and that it is not seldom associated with true neoplastic changes—that is, the decay which gives rise to cysts gives rise to neoplasms. "There is in mammary glands which have long ceased to be active, and those of women past child-bearing, a

* Bryant: *Op. cit.* p. 121.

cystic degeneration of their ducts and glandular structure which may simply remain as such or take on active changes. Under the latter circumstance, a cyst or many cysts, may either enlarge so as mechanically to cause trouble or become the seat of intra-cystic, adenomatous, sarcomatous, or carcinomatous growth which will run the usual course of such tumours." . . .

"If, clinically, simple cystic tumours of the breast are fairly common, pathologically they must be pronounced to be comparatively rare, for it is, I think, indisputable that in the majority of cystic tumours of the breast, of whatever character, of duct cysts, gland cysts, or connective tissue cysts, *some solid element can usually be found proliferating from their lining walls, either in the shape of a small, sessile, or pedunculated outgrowth, or of a solid tumour composed of glandular, epithelial, or connective tissue elements.*"* That all varieties of mammary neoplasms should thus be associated with the structural disorganizations of cystic disease will tend greatly to strengthen us in the belief that neoplasia proceeds out of the conditions posited by our hypothesis.

The conditions of benign tumours of the breast—the adeno-fibromata—are less easily understood. Of 100 cases observed by Mr. Bryant,

"27 cases were first discovered between puberty and the age of 20; that is, during the developmental stage of the breast's life.

35 cases appeared between 21 and 30 years of age, or during the period of its functional perfection.

22 cases appeared between 31 and 40, during the period of its maturity.

13 cases appeared during 41 and 50, and

3 cases appeared in women over 50, or during the period of its functional decline.

46 of these cases occurred in single women;

39 in the married and prolific;

15 in the married and sterile."

"Single women during their prime are consequently most prone to

* Bryant: Op. cit. pp. 250, 268.

be attacked by these growths, and the married and prolific are the next; the old maid and the married and sterile woman being comparatively free from these benign tumours."

Is it not thus shown that benign tumours of the mamma are related rather to exuberance than to decline of tissue-life? Such certainly are the superficial appearances. In reality the facts do not yet afford such an insight into the causes as will suffice for more than tentative conclusions. But I think the evidence requires the conclusion that adeno-fibromas originate, as there is ample reason to think the cancers do, in histogenic dissolution, only that the conditions of the dissolution are different. It seems probable that in single women, under the age of twenty years, irregular sexual excitement unaccompanied by the healthy exercise of function is the leading cause of these tumours. Such excitement in some unknown way diminishes the vital power of small groups of gland-elements. It may be recalled how frequently the breasts of young unmarried women are subject to functional perturbations, and the cases of adenoid tumour often show that the causes do not differ in essence and kind from those which produce cancer (see the following cases). It will be perceived from the foregoing table that married and prolific women furnish a large proportion of the cases, a fact in evidence that the waste incidental to use is the circumstance out of which the disease originates.

The structural superiority of the adenoid neoplasm is ascribable to the youth of the subject or to the more superficial character of the dissolutional change or to both combined. The limited extent of the changes is similarly explicable. Though there may be present in one breast two or more centres of growth, and the tumour may be very large, the surrounding gland remains healthy. On the other hand, in cancer the appearances almost compel the conclusion that extensive portions, sometimes the whole organ, undergoes histogenic dissolution. And the usually slow growth of the benign tumour harmonizes with this view; the physiological resistance of the tissues is at a maximum. "The increase of

adenomas is, upon the whole, less rapid than that of any other neoplasm of the breast.”*

Cases Illustrative of the Facts Interpreted.

CASE 67.—*Sarcoma of the right breast following abscess in that breast.*—“E. S., aged 43. She is a married woman and has only one child, eleven years old. Her general health has been good. After her child was born she had an abscess in the right breast, which ran its course and got quite well, leaving behind some slight induration. She states that the first sign she had of any tumour was four years ago, when she noticed a lump on the site of the abscess.” (*Purcell: The British Journal of Gynæcology*, p. 442.)

CASE 68.—*Adeno-sarcoma (spindle-celled) of breast.*—“F. C., a married charwoman, aged 50, the mother of five children, all of whom she suckled, came with a tumour in the upper part of her right breast, which she had accidentally discovered six weeks previously. It was then the size of a pigeon’s egg, smooth and painless. The skin over the tumour was healthy. Nipple natural.” (*Bryant.*)

CASE 69.—*Cystic degeneration of the breast, with enlargement of one of the cysts, and the development of an intra-cystic adeno-fibromatous growth; removal of the growth; twelve years later carcinoma of the cicatrix.*—“A healthy widow, aged 30, with one child ten years of age, consulted Mr. Birkett in October, 1859, for a small painless swelling, situated in the clavicular lobe of her left breast, which had been growing for seven months. The tumour was in a measure pear-shaped, with its narrow end near the nipple, nodular and elastic. Pressure upon it caused a few drops of a clear, yellow, viscid albuminous fluid to exude from the nipple, which was natural. The axillary glands were not enlarged. In December, 1859, the tumour was excised with some of the breast gland, and the patient recovered. On section the tumour was found to be formed of a cyst, which contained serum, and communicated with a duct near the nipple. Throughout the tissue of the lobe removed, and of the gland structure exposed by the incision, were small cysts, containing intra-cystic growths. There was no distinct, well-marked, limited

* Gross: *American Journal of the Medical Sciences*, 1879, p. 459.

envelope around the tumour, but the cyst and all the new growths were so closely identified with the ordinary tissue of the breast, that it was absolutely necessary to cut its structure in order to remove effectually the whole of the tumour. The intra-cystic growths were composed of the cæcal terminations of gland-tissue and fibre elements, the former loaded with epithelium. The patient remained well for eleven and a half years, when a carcinomatous tubercle appeared in the scar, which enlarged and ulcerated." (*Bryant.*)

(Here the course of events reveals in a very objective manner the doctrines that have been inculcated. Disease of the epithelium of the acini leads to cystic formation and from the degenerate tissues there grows out a neoplasm fully developed and of glandular type. As yet the patient is comparatively young, and the devitalization of the tissues that gave birth to the new growth is not profound; but it becomes so with the increase of years, and a carcinoma at last springs from the spot of least viability—the scar of an operation wound.)

CASE 70.—*Cystic-duct sarcoma of the breast which never secreted milk.*—"Mrs. G., aged 45, the mother of one child, seventeen. She had suckled with her right breast, but not with her left because she had no milk in it, and the nipple was retracted. For six years she had had a discharge of a clear fluid from the retracted nipple of the left breast, and which at the catamenial periods was increased; the fluid at times was like 'treacle water.' Three months ago this flow stopped and a lump appeared. A tumour the size of a walnut exists in the centre of the breast beneath the nipple." (*Bryant.*)

CASE 71.—*Cystic sarcoma of the right breast.*—"Eliza A., aged 45, a governess. Patient is a florid-looking woman and apparently healthy. In January, 1883, one year before admission, patient first noticed a pale brownish discharge from the right nipple. It lasted three months and was increased during the menstrual periods. In March she noticed a lump, the size of a small marble, on the upper and inner part of her right breast. This increased visibly during her menstrual periods." (*Bryant.*)

CASE 72.—*Cystic disease coming on after prolonged suckling and*

followed by cancer.—"S. C., aged 44, the mother of one child, which she suckled for three years up to six weeks ago, applied to me on April 25th, 1865, for a soft swelling the size of an egg in the outer lobe of her right breast. It was fluctuating, and had been coming two months. On August 17th the cyst burst and discharged a yellow serous fluid. In January, 1866, patient reappeared with the breast generally infiltrated and fixed to the chest." (*Bryant.*)

(These cases prove to us that while cystic disease renders the tissues apt for sarcoma and cancer it is itself induced by conditions that may lead directly to sarcoma and cancer. The intimate nature of cystic disease requires to be worked out, but we may note Mr. Bryant's conclusion that the glandular change is a general one and begins in the epithelium of the ducts and acini (op. cit. p. 289). In cases 70 and 71 it was preceded by discharge from the nipple, and the discharge was augmented with the menses.)

CASE 17.—*Rapidly growing sarcoma of right breast, associated with atrophic scirrhous of the left breast of twenty years' growth, and lipoma of the side.*—"Mrs. T., aged 64, a very healthy-looking woman, consulted me in 1882 for an ovoid, smooth, semi-elastic tumour, the size of a cocoa-nut, which occupied the position of her right breast. She was the mother of three children, all of whom she nursed with the left breast, but not with the right, as it was hard and gave no milk. The tumour had been growing for about eight months, slowly at first, but rapidly for the last three months. The breast was lost in the tumour. . . . I regarded it as a sarcoma. In the left, or opposite breast, was a typical atrophic carcinomatous tumour, which had existed for sixteen years. The breast was contracted up into a stony mass.

"Over the left hip there was a lipoma the size of a fist, of twenty-five years' growth." The tumour in the right breast was removed and recurred sixteen times. (*Bryant.*)

(The induration of the right breast which preceded the development of sarcoma on that side was due to some perversion of function, perhaps from use of the corset. It may be inferred that these conditions induced a state of weakness in the connective elements of the gland, while other conditions set

up weakness in the parenchymatous elements of the opposite breast. The indolent character of the scirrhous tumour and the localization of the recurrent sarcoma may be held to signify good local and constitutional resistance. Each one of the recurrent growths was fenced off by a capsule of connective tissue out of which it was readily enucleated.)

CASE 74.—*Spindle-celled sarcoma of the male breast.*—"D. M'L., æt. 37, labourer, a strong, healthy-looking man, was admitted with a large ulcerated and pulsating tumour of right breast of seven years' duration. The tumour, on admission, was 22 inches in circumference, hard, lobulated, incapsuled, and running more or less freely on subjacent tissues, with great and foetid discharge from surface. Seven years ago patient received a blow on the breast from a heavy piece of iron, causing a wound which the patient describes as a *hash*. He paid little attention to it at the time, but from the irritation of sweat and a woollen semmit, it cankered, and ultimately a lump formed which made very little progress till he received a second blow on the same spot. After that he had several blows at different intervals, with the effect of a more rapid increase of growth after each injury." (*Muir: Glasgow Medical Journal*, vol. xiv. p. 157.)

(Hereafter we shall see that violence often repeated is among the most efficient causes of malignant disease.)

CASE 75.—*Adeno-fibroma of breast; excision; second tumour discovered by the incision made to remove the first; removal of second; recovery.*—"Harriet P., aged 30, single, a servant, came under my care on September 23rd, 1874, for tumour in her left breast. It had appeared nine months previously as a small movable lump, which steadily increased. At present it measures three inches by two, is situated below the nipple, is movable, nodulated and firm. On the 25th an incision was made into the tumour. When this was done, a second tumour was discovered placed deeply in the gland beneath the one that had been removed." (*Bryant.*)

CASE 76.—*Adeno-fibroma of the breast, with retracted nipple.*—"In 1878 I removed from the left breast of Miss N., a healthy girl, aged 18, an adeno-fibroma of six months' growth, which was placed in the centre of the breast, and gave rise to retraction of the nipple." (*Bryant.*)

CASE 77.—“A. W., coloured, æt. 53, widow. Eighteen years ago, while washing, she ran a needle into the right breast at the nipple; it caused but little pain, and she had forgotten it until two months after she noticed a slight discharge, which was bloody, from the nipple. Two or three months later a hard lump was found in the breast on examination. The discharge ceased after a time, but the breast steadily and very slowly increased. The patient was married twenty-five years ago; has had three children; all prior to the breast trouble.” (*Longstreth: Philadelphia Medical Times*, vol. x. p. 217.)

(Shows that, like cancer or sarcoma, adenoma may be determined by injury, and also, like cancer, the appearance of the tumour may be preceded by discharge from the nipple. A serous or bloody discharge from the nipple is not rarely the forerunner of cancer, and it implies the existence of a disintegrative process. Such is the process of histogenic dissolution.

CASE 78.—*An adenoma of forty years' standing undergoes cancerous degeneration.*—“E. T., aged 58, has been the subject of a tumour of the left breast during forty years. She first detected a lump in the left breast, above the nipple, of the size of a walnut. Her impression is that the tumour was quite movable for many years, and that the skin could be lifted off it. During the last twelve months the tumour has enlarged, very rapidly during the last three months, associated with darting, shooting pains, and the oozing of a yellowish clear fluid from the nipple. The whole gland appeared to be infiltrated more or less with scirrhus, the skin being discoloured and firmly adherent over the greater part of the tumour. There were two or three enlarged axillary glands.” (*Maunder: Lancet*, 1867, ii. p. 293.)

CASE 79.—*Adenoid tumour of the breast of forty years' duration.*—“Mrs. W., æt. 77, a small active-looking woman of very spare frame, and bearing an undistressed appearance. Forty years ago, after a slight blow on the right breast, a small movable tumour formed in the upper part above the nipple. This, the first swelling, became after the lapse of years lost in a general enlargement of the breast, but the growth of the part was by no means remarkable until three years since. For many years it was entirely painless.

She was married nearly fifty years ago, was never pregnant, had regular menstrual periods, and on their disappearance observed no change in her health or in the breast. The situation of the right mamma is occupied by a vast tumour having a girth of thirty-six inches." (*Pemberton.*)

(Thus we learn that as the viability and physiological resistance of the tissues diminishes with the arrival of new conditions, indolent tumours tend to become active.)

§ 28. *Cancer of the Uterus.*

Our next effort must be to draw some truthful conclusions as to the causes of cancer of the uterus, and, as before, a perception of the facts will be the first step.

The mean age is nearly that observed in cancer of the breast, about forty-five years. In a large group of cases *

16 patients were from 20 to 29 years of age.					
195	„	„	30 to 39	„	„
272	„	„	40 to 49	„	„
192	„	„	50 to 59	„	„
65	„	„	60 to 69	„	„
7	„	„	70 to 79	„	„
1 patient was	„		80 to 85	„	„

The disease is only exceptionally met with among unmarried women. Of fifty-four hospital patients observed by Dr. Graily Hewitt† there was no note in five cases as to whether the patients were married or not, but in forty-eight cases the patients were married, and in one case the patient was single but had had a child. Further on Dr. Hewitt adds: "I have recently looked over my notes of cases observed in private practice during six years (1873-79), twenty-seven in number. There is not one of the twenty-seven in which the patient was single." The observations of others are in keeping with this. "Of ninety-one cases eighty were married, and ten were

* Hofmeier: *Zeitschrift für Geburtshülfe und Gynäkologie*, B. 7, 8.

† Diseases of Women.

widows, or were separated from their husbands. One woman was single, but she had been delivered of a child at the full term, seven years prior to the occurrence of any symptom of malignant disease.”* Among thirty-seven cases investigated by Dr. J. Williams† there were none in single women, and of those observed by Dr. F. Winckel‡ only 1·7 % of the patients were unmarried, but two-thirds of these had borne children.

A characteristic circumstance of this disease is the marked fertility of the patients. Of the whole number of Dr. Tanner’s cases “twelve had never been pregnant, one had had several children, and twenty-three had aborted once or oftener. Then there were seventy-nine women who had had 497 pregnancies amongst them, or an average of about $6\frac{1}{2}$ to each.” The average in the general population is, I believe, about four. The observations of others are not widely different. In 143 cases the average was 5·6 (*Roger Williams*); in 580 cases 5·1 children (*Gusserow*); in another series 5·6 (*Winckel*).

There is not only a correspondence between uterine and mammary cancer in the fecundity of the patients, but also in the regularity of the function of menstruation and the state of the general health. “In 157 out of 170 cases the manner in which the menstrual function was usually performed was made the subject of special inquiry. In 131 cases it was performed in all respects naturally, from the time of its complete establishment until the commencement of the disease.”§

Often the patients are in good and even blooming health at the time of observation, but there is also not infrequently a personal history of hardship and privation. “Out of 137 cases the previous health was good in 104 (with no serious illness since youth in seventy); indifferent in twenty-one and bad in twelve.”|| “The antecedent condition of system which has

* Tanner: A Clinical Report on Cancer of the Female Sexual Organs.

† Cancer of the Uterus.

‡ Lehrbuch der Frauenkrankheiten.

§ West and Duncan: Diseases of Women.

|| Middlesex Hospital Reports, 1885, p. 80.

been present in the cases which have fallen under my own notice has been various. In some, the individual was in apparently good health, but in many the state of things was the reverse. Prolonged anxiety, depression of the general health, and an evidently low state of vital power, I have certainly been induced to regard as rather frequent antecedent conditions. Great debility and prostration from prolonged excessive lactation has been apparently connected with the occurrence of uterine cancer in several instances under my own observation.”* “Of 103 uterine cases in which preceding causes of mental or physical nervous depression (trouble or very hard work) were sought for, fifty-five gave a history of preceding mental trouble (often combined with hard work), ten of hard work alone, while ten gave doubtful replies.”†

Leucorrhœa is a common antecedent and a common accompaniment. “A white or yellow discharge was present in every case in a greater or less degree with one exception; it had been present in some long before any evidence of the disease existed.”‡ Latterly, as by Ruge and Veit,§ stress has been laid on the connection between erosion of the cervix and cancer of that part. Into the meaning of this connection we shall inquire presently.

Many gynæcologists are disposed to give to lacerations of the cervix, occasioned during parturition, a prominent place among the direct causes. These have been made to include also the irritative influence of gonorrhœal discharges.

Of much moment are the facts about the localities of the disease. The results of Dr. J. Williams’s research show that cancer of the uterus may begin in three situations: in the squamous epithelium of the portio-vaginalis; in the follicles of the cervix at any part; and in the follicles of the mucous

* Graily Hewitt: *Op. cit.*

† Snow: *Lancet*, 1881, v. ii.

‡ Williams: *Cancer of the Uterus*.

§ *Zeitschrift für Geburtshülfe und Gynäkologie*, B. 7 and 8.

membrane of the body of the uterus. As a starting-point the portio-vaginalis is prominent in frequency, but cases are seldom seen before the cervix has become involved. Hofmeier states* that in 812 cases the disease began in the portio-vaginalis in 236, in the cervix in 181, and in the body in 28; in 367 the particulars were not given. Dr. Williams describes 8 of the portio-vaginalis, 19 of the cervix, and 3 of the body of the uterus, and remarks that "cancer of the vaginal portion begins in the stratified epithelium on the vaginal surface, or in the transitional epithelium of the os externum. Cancer involving this part is common enough; indeed, most of the cases of so-called cancer of the cervix are instances of cancer involving this part, but not originating in it." From which we must infer that the disease begins oftener in the portio-vaginalis than is indicated by the cases observed.

Is it possible to join these facts together by a consistent rationale? Bearing in mind the nature of neoplasia as here understood, let us consider, in the first place, the local features of the disease. Clearly, the causes of cancer of the body of the uterus are not likely to be identical with the causes of cancer of the cervix and portio-vaginalis. Besides the differences in local circumstances, the disease of the body is often diffuse, occupying the entire inner surface of the uterus; the disease is less localized than when situated elsewhere. "Cancer of the body may be diffuse or circumscribed. The diffuse form is much the more common; indeed, I have not met with an instance of the circumscribed."† Wilks and Moxon say:—"There is a more rare form of disease where we find the new growth has sprung up all over the surface of the uterus. . . . We have seen the whole mucous membrane covered with a soft carcinomatous growth." But when the affection begins in the portio and cervix, it is perhaps always circumscribed. The posterior cul-de-sac of the portio-vaginalis and the posterior lip of the cervix are very frequently the seats of origin. "Of twenty-

* Loc. cit.

† Williams: Cancer of the Uterus.

five cases, the whole cervix was involved in nine when first seen, and it was not possible to discover the starting-point of the growth. *In eleven the cancer had clearly begun in the lower part of the cervix.* So that, although the upper part of the cervix is by no means uncertain as the starting-point of cancer, yet the lower half appears to be a by far more favoured site. . . . Of twelve in which the disease had begun in the lower part of the cervix, the posterior lip was alone or chiefly affected in six, the anterior in three, and the right commissure and lips in two, leaving the left commissure free. So that cancer appears to show a preference for the posterior rather than the anterior lip of the uterus." (*Williams.*) There are, then, two distinct forms of cancer of the uterus; one, a somewhat rare form, liable to commence over the whole surface of the mucous membrane of the body, and the other, the common form, most liable to commence in the posterior cul-de-sac of the portio-vaginalis, in the lower part of the cervical canal, and on the posterior lip. Is there anything in the different life-conditions of the tissues implicated that will account to us for these two forms of the same disease? What can be the circumstances determining the great frequency of cancer in the portio-vaginalis and lower half of the cervix? I think the evidence affirms that cancer of these parts has the closest possible connection with sexual intercourse. We may inspect the facts severally as they lean to this assumption.

We have seen that it is a rare and exceptional circumstance to meet with cancer of the uterus in the unmarried, and when so met with, almost invariably the patients are positively known to have been impregnated. We are quite without satisfactory grounds for thinking that cancer of the uterus has ever been encountered in a virgin. Though on this point the evidence already adduced is conclusive, we may add the observation of Dr. Emmet that he has "never known a woman to have any form of epithelial cancer of the uterus unless she had at some time been impregnated."

Next we find that cancer of the uterus is most common in prolific women; an average of 5·6 children is a high average, and is

one established by a consensus of observations. Now extreme fertility, besides being favourable to exhaustion of the uterine tissues and to lacerations of the cervix, will, in general, go with a free indulgence in sexual pleasures. Of this we may feel certain, for sexual appetite is the explicit assertion of reproductive capacity. If the truth lies in this direction, the disease, we may anticipate, will occur frequently among prostitutes. Such appears to be the case, though there is wanting more evidence than that extant. Dr. Hawkes Tanner has dismissed this point with the indefinite statement that prostitutes are neither more nor less than others subject to the disease. Winckel says that prostitutes are not particularly liable, but Glatzer, corroborated by others, is quoted by Billroth* as saying that of 365 patients, 91 were prostitutes. Among "365 an Gebärmutterkrebs zu Wien verstorbenen Frauenzimmern 91 (also nahezu 25 %) als 'Handarbeiterinnen' bezeichnet, da sich nach ihm unter diesen Namen die Lustdirnen in Wien anzumelden pflegen, schient ihm diese Klasse ein verhältnissmässig starkes Kontingent für die gedachte Krankheit zustellen."

But if cancer of the portio and cervix is causally related to indulgence in sexual intercourse, in what way does sexual intercourse operate? By excitation and ultimate exhaustion of the tissues whose function it is to receive the seed of the male. Observe, now, how all the facts will be vivified by so looking at them. In sexual congress, the semen is ejected upon the portio-vaginalis and os uteri, and especially upon the posterior wall and lip; the very parts, in all probability, where cancer oftenest begins. The tissue-units which succumb to the influence of the semen are the epithelial cells of these parts; the surface epithelium of the vagina and the follicular epithelium of the cervix. These structures are required to elaborate a secretion which probably serves the purpose of a vehicle for the transmission of spermatozoa to the body of the uterus. Under repeated stimulation the life of the cells is drained away, and they dissolve histogenically.

* Handbuch der Frauenkrankheiten.

Thus conceiving cancer of the portio-vaginalis and cervix to arise from excessive functional activity of the epithelial tissue we are enabled to understand the frequent association of the disease with erosion of the external os and are further enabled to understand the histological changes peculiar to erosion. Erosion is not, as the term implies, a disintegrative change but is in reality a glandular hypertrophy. Dr. J. Williams describes it as "like an extension of the mucous membrane of the cervical canal through the external orifice on to the lips, which are in health covered by stratified epithelium. In cases of erosion the glands of the lower part of the cervix are greatly enlarged and multiplied. They enter deeper into the cervical wall than they do in health, and their interior is frequently covered by papillary processes. The glands are lined by columnar epithelium which is usually like the epithelium of the cervical follicles. The wealth of glands in an erosion is usually great; they branch and divide and form clusters of follicles having one tubular outlet." Is not such overgrowth of glands precisely what may be looked for as the consequence of undue functional activity? We saw when considering cancer of the tongue how the disease in this organ is very often preceded by leucoma or smoker's patch: an epithelial hypertrophy responsive to the irritation of tobacco-smoke. Erosion is a strictly analogous change. (See p. 92.) Exactly in what proportion of cases it is directly related to coitus has yet to be ascertained, but I think we may venture to assume a large proportion.

White and yellow discharges (leucorrhœa) as just now noted generally precede and accompany cancer of the uterus, and these discharges imply great activity of the uterine follicles; but leucorrhœa has causes independent of coitus.

It is worth attention that early in this disease coitus is sometimes followed by discharges of blood *per vaginam*, a symptom showing how the uterine tissues are stimulated by the act of copulation; and Walshe says that he has known women afflicted with this disease to take refuge in hospitals from the importunities of their husbands. (See appended cases.) This helps to substantiate the view that sexual inter-

course is one and an important cause of cancer of the cervix and portio.

Thus the facts plainly warrant the first place being given to sexual intercourse—this is entitled to rank as the essential cause. There are, however, numerous contributory conditions. Multiple pregnancies especially will contribute both directly and indirectly. In Hofmeier's cases seventy-six patients had had over ten pregnancies. And out of 150 cases tabulated by Dr. West there were only two patients "whose pregnancy had issued merely in abortion." Moreover, of these patients in thirteen instances the disease manifested itself immediately after the last pregnancy. Therefore we may safely say that many pregnancies with their numerous contingencies settle the development of the disease in a large proportion of cases. Inflammations, ulcerations, and lacerations of the womb, deserve to be specially mentioned as being in secondary connection with gestation and parturition. Doubtless sometimes, perhaps often, impure sexual intercourse—gonorrhœal and venereal infection—will be decided factors. Lastly the ages of the patients must not be left out of sight.

After the foregoing sections no difficulty will be felt in reconciling with this interpretation the facts given in connection with menstruation, the general health, and the conditions of life affecting the whole system (pp. 84 and 110). And the facts just reviewed speak with considerable force in favour of the view I have advanced that cancer of the sexual system in women is not unconnected with the established monogamy of civilized countries in succession to the polygamy of an earlier and more primitive social state (p. 138).

Cancer of the body of the uterus has been seen to differ from cancer of the cervix and portio-vaginalis. It is much less common, is often, if not usually, diffuse, and is met with in older subjects. Unfortunately these facts will not permit of settled opinions as to the cause of the disease. That form in which the entire mucous membrane suffers, must obviously arise from causes having a somewhat general distribution.

The tubular glands of the mucous membrane or *glandula uterinæ* are, it is acknowledged, the structures involved in the genesis of cancer of the body and these glands are believed to be subjected to great changes at each menstrual period. "During menstruation the thickness of the mucous membrane increases, the epithelium of the surface and of the greater part of the glands being destroyed by fatty degeneration, and finally altogether detached. Afterwards its restitution takes place from the remnant in the depth of the glands."* It may hence be supposed that in certain persons inordinate activity of the uterine mucous membrane from frequent and prolonged menstruation and pregnancy will lead to the partial dissolution which we assume underlies neoplastic disease. Ruge and Veil assert that cancer of the body of the uterus is associated with late menstruation, and the average age of patients is higher than in cancer of the cervix. "The disease is rare under fifty and before the menopause."†

Cases Illustrative of the Facts Interpreted.

CASE 80.—*Cancer affecting the posterior lip of the os and posterior wall of the vagina.*—"M. G., aged 42, married. Admitted to the Cancer Hospital, October 16th, 1885. The mother of six children; is a thin delicate woman, and has been losing flesh. In April last believed herself to be pregnant; in July had a flooding and bad uterine bleeding a week prior to admission. These losses and her general wasting and delicate state of health were her sole reasons for seeking advice. No history of cancer in her family. On examination, per vaginam, an epitheliomatous growth was found occupying the posterior lip of the os and extending posteriorly on to the wall of the vagina, the uterus being freely movable; no further infiltration of the disease discovered."

CASE 81.—*Cancer of the os and cervix.*—"M. R., aged 42, married. Has had nine children; the youngest is now nineteen months old. Has recovered well after her confinements, and always enjoyed good health until ten months ago, when she first noticed a discharge from the uterus.

* Klein : Elements of Histology, p. 267.

† Williams : Cancer of the Uterus.

“An examination, per vaginam, reveals the whole of the lower segment of the uterus enlarged with an irregular, hard, and nodulated outline, and but little sensitive. The os and the whole of the cervix uteri appear to be implicated in the disease; but the finger can be passed quite round in the cul-de-sac of the upper extremity of the vagina.” (*Sir J. T. Simpson.*)

CASE 82.—“A. S., aged 34, married eleven years. Has had three children, all healthy. Up to this present year she has enjoyed very good health, and has been in the habit of working very hard at washing and cleaning. In April last (after a week of unusually hard work, in the course of which she was often lifting heavy weights), while she was menstruating, menorrhagia supervened, and continued in various amount for five months. She states that she was robust before her illness commenced. A vaginal examination shows extensive disease of the os and cervix uteri, with considerable loss of substance.” (*Ibid.*)

CASE 83.—*Uterine cancer; hæmorrhage after coitus.*—“Patient 40 years of age; had had two children and some miscarriages. Her husband was away for six months and returned a fortnight ago, and she had observed a slight loss of blood after coitus since—but at no other time. The growth was a glandular cancer. The glands of the cervix were greatly increased in size and number, and many of those on the surface had not become cancerous. The mucous membrane of the lower part of the body was thickened and villous, and its glands were greatly enlarged, and showed what is never seen in glands of the body in health—namely, frequent division with numerous papillæ on their inner surface. They were like the glands of an erosion.” (*J. Williams.*)

CASE 84.—*Cancer of the portio-vaginalis.*—“Patient 39 years of age; married eighteen years. Has had one child, seventeen years ago, and one miscarriage a year later. She says she has had inflammation of the womb three times, and has suffered slight scalding with micturition, since she had rheumatic fever nine years ago. For nine months there has been pain during, and hæmorrhage after, sexual congress.” (*Ibid.*)

CASE 85.—“Patient 42 years of age, married. She has always been a strong healthy woman previous to her present illness. At the beginning of her illness had discharge of blood from vagina

during micturition; this discharge would last for a week or a fortnight, and then cease for a time. Only appeared during micturition. For a long time has been subject to bleeding after coitus. But in August, 1883, connection was followed by a large flooding. Since that time hæmorrhage has been almost continuous. Menstruation at fifteen, regular, and never painful. Married at 34; one child." (*Ibid.*)

(It is shown by the first of this group of cases that the influence of the conditions which set up the precancerous state called "erosion" may extend to the body of the uterus.)

CASE 86.—*Uterine cancer; the patients twice married.*—"Patient 31 years of age. First noticed a yellow discharge three years ago. Menstruation at fifteen, regular. Has had rheumatic fever three times. Has been twice married, first at eighteen and again at twenty-nine. One child. No miscarriages. Cervix had been lacerated on right and left sides." (*J. Williams.*)

CASE 87.—"Patient 41 years of age, married; previous health had been good. Menstruated at sixteen, regular, free. Married at sixteen and again at twenty-five. Seven children and no miscarriages. Twins twice. The patient says that for six months previous to September last the interval between the periods had been gradually decreasing until in September it was only four or five days." (*Ibid.*)

§ 29. *Myoma and Sarcoma of the Uterus.*

Next among tumours of the uterus to claim our attention is the myoma. It is essentially one of the benign neoplasms, and derives its importance from the exceeding frequency of its occurrence and the severity in many cases of its effects. The myoma is a tumour of the muscular tissue of the uterus, and although met with in various stages of development and degeneration is practically a growth of fully-developed tissue, and in correspondence with this occurs at an earlier age than cancer of the uterus. In 919 cases collected by Gusserow,*

* Billroth's Handbuch der Frauenkrankheiten.

15	patients	were	under	20	years	of	age
156	„	„	from	20	to	30	
357	„	„	„	30	to	40	
338	„	„	„	40	to	50	
36	„	„	„	50	to	60	
12	„	„	„	60	to	70	
5	„	„	above	70			

These results are substantially sustained by independent observations and from a consideration of the whole the conclusion issues that myoma most commonly appears between the ages of twenty-five and forty-five.

It has been asserted that unmarried women are more liable to these tumours than married women. This, however, is quite contrary to the fact. "Of 96 women affected with non-pedicated fibrous tumours, 82 were married."* Of 180, 152 were married.† The papers of Professor Winckel‡ and Professor Roehrig§ also prove the inaccuracy of the opinion that celibacy favours the disease. To quote from an excellent *résumé* of these papers,|| "married women are decidedly more predisposed to this affection than unmarried, *i.e.* than those who can satisfy their sexual instinct either rarely or not at all."

In appreciating the influence of fecundity it should be remembered that uterine myomas are a cause of sterility. If we duly allow for this, frequent conceptions appear to be favourable. Dr. Emmet says that "on reaching a certain stage of development the tumour unquestionably caused a number of miscarriages, and finally a condition of permanent sterility. But before the fibrous growths existed, or while yet

* West and Duncan: Diseases of Women.

† Meadows: *Lancet*, 1873, vol. i. p. 657.

‡ Volkmann's *Sammlung Klin. Vorträge* No. 98.

§ *Berliner Klin. Wochenschrift*, 1877, Nos. 30, 31, 34, 35.

|| *Medical Times and Gazette*, 1879, vol. i. p. 10.

in their incipency, these women were unusually prolific. This is true, since the average number of impregnations for them is quite as great as that taken on the general average. Thus, 1249 fruitful women under observation had given birth to 3550 children at full term, and in addition, had miscarried 1009 times, making 4559 impregnations, or an average of 3.57 pregnancies for each woman.”* These observations are borne out by those of Winckel and Roehrig, but the favourableness of functional exercise of the uterus as a condition of uterine myoma is shown more decidedly by Dr. Meadows.† Among 152 married patients “45 were sterile and 94 fertile. Of the latter 46 aborted, the total abortions being 105. The number of children born was 454, and the total number of pregnancies was 559, giving an average of nearly six pregnancies to each. Further, of the 152 who were married, the number of years of married life is stated in 128, and the total number of years amounts to 1937, giving an average of 15 years and a fraction to each.”

Passing now to the facts as to localization we see at once that this disease is not, like cancer of the uterus, confined more or less exclusively to some limited portion of the mother tissues. It is true that myoma seldom grows from the muscular tissue of the cervix and most generally from that of the body, yet it may grow from any part of the body. It may appear upon the peritoneal surface, in the substance of the walls, or within the uterine cavity. Of 334 myomas, 27 were situated in the cervix, and 307 in the body of the uterus. Of 307 in the body, 106 were interstitial, 128 subserous and 24 submucous.‡ The observations that have been made upon the relative liability of the different divisions of the uterine wall are not as yet conclusive. We may say of its distribution among the elements of the uterine tissues that myoma affects any portion of the muscular substance, but usually that of the body. Now and again the whole of the muscular substance

* The Principles and Practice of Gynæcology.

† *Lancet*: Loc. cit.

‡ Billroth: Op. cit.

may be transformed into tumours. Dr. Meadows describes such a case as follows: "I have seen the uterus completely studded with them, both within and without, so that on making a section of the uterine wall the surface looked almost like the skin of a person suffering from small-pox; so numerous were the tumours that it was literally impossible to count them. They varied in size from that of a millet seed, or even less, to that of a small walnut."

Before we pursue more particularly this inquiry into the etiology of uterine myoma it will be useful to see what general conclusion is warranted by the facts already reviewed. First to recall the conclusion expressed as to the causation of mammary adenoma. The neoplasm we are considering is in many of its features to cancer of the uterus what adenoma of the breast is to cancer of that organ. Uterine myoma and mammary adenoma are both highly organized growths and both are classed among innocent tumours. They are comparable also in their conditions; both tend to appear at an earlier period of life than cancer: they are relatively frequent among young single women. Besides this, both these forms of benign tumour are favoured by marriage and fecundity. Being alike in these ways, may it not therefore be assumed that they are alike in their deeper nature and conditions? In speaking of the probable etiology of mammary adenomas it was said that they arise out of the histogenic dissolution of limited groups of cells, and that the dissolution is related to glandular activity in connection with menstruation, sexual excitement, and child-bearing. The large number of married and prolific women afflicted with mammary adenoma forbade the supposition that the disease was due to glandular inaction. These conclusions are, I think, applicable to uterine myoma. The disease is probably dependent on the uterine changes of function and structure incidental to sexual excitement, the catamenial periods, pregnancy, and other conditions, and the root-change is a partial dissolution by histogenesis of definitely and narrowly circumscribed tracts of muscular tissue; we have seen that a single uterus may contain innumerable distinct

tumours, and it has been observed of their mode of growth that the "fibres encompass a centre from which the disease appears to have sprung."* Let us now see if there is for this view any further confirmatory evidence.

From a study of cases coming within their own observation, Professor Winckel and Professor Roehrig assign as causes of the disease conditions clearly competent to induce a partial dissolution of portions of the uterine tissue. (See appended cases.) These observers refer to accidents of various kinds as the true determinants of the tumours. Thus the disease may be caused by the bruising of a retroflected uterus in coition during early married life; by falls and blows while the subject is pregnant; by miscarriages and the accidents of childbirth; by want of care at the menstrual periods and by metric inflammation. Cases are also referred to gonorrhoeal inflammation and to medication of the uterus by means of injections and the use of intra-uterine stems. Lastly the disease was met with in persons who had suffered severely from fevers and acute rheumatism, and from uterine congestion consequent on heart disease. According to our conception of its intrinsic nature, uterine myoma may quite naturally succeed to such conditions.

Sarcoma of the uterus, which requires a few concluding words of notice, is seldom seen and, as yet, little has been learnt as to the circumstances of its origin. The age of greatest frequency is from forty to fifty years. It is very probable that many cases are the result of histogenic dissolution in the substance of a myoma. Emmet, writing of this neoplasm, says: "I have seen but seven cases where I could be positive of the diagnosis, all with one exception, occurring among women who had never borne children; and in five the disease developed in connection with supposed fibrous growths long previous to the appearance of the sarcoma." (For cases of sarcomatous degeneration of uterine myomas see *Edinburgh Medical Journal*, Jan. 1882, and the 34th volume of the Transactions of the Pathological Society.)

* Wilks and Moxon: Pathological Anatomy.

Cases Illustrative of the Facts Interpreted.

CASE 88.—“A lady, 34 years of age, had already given birth to two healthy children, and suffered no disturbance before, during, or immediately after the pregnancies. Ten weeks after the last confinement a Newfoundland dog unexpectedly sprang upon her, and so frightened her that she aborted, and after abundant and irregular hæmorrhages did not become pregnant again. Two years afterwards she noticed a symmetrical quickly growing enlargement of the abdomen, which her family physician took to be a gravid uterus, until at the ninth month it was discovered to be a fibromyoma.” (*Roehrig: Berliner Klin. Wochenschrift*, 1877, No. 34.)

CASE 89.—“A lady had for five days an extraordinarily painful labour (face presentation) and afterwards rigors and violent puerperal fever. From the last day of her confinement she experienced a sensation of pain in the left side, and there two years later a tumour was discovered.” (*Roehrig.*)

CASE 90.—*Uterine myoma following Suppression of Menses.*—“An unmarried lady, aged 31 years, well known as a landscape painter, when menstruating, threw herself upon wet grass and fell asleep. When she awoke she felt splitting pains in the body and a weakness in the right leg, while the menses, which according to rule should have continued for another day, ceased at once. The menses returned after a period of ten months, but from that time became irregular. The weakness of the lower extremity continued in spite of electrical and thermal treatment, and there were exacerbations accompanied with colic at each menstruation. Three years after the mishap a uterine tumour was diagnosed.” (*Roehrig.*)

CASE 91.—“A newly-married couple ascended the Righi and Mount Pilatus on two successive days, the lady menstruating at the time. The result was that she was laid up at Lucerne with metritis, and for three years afterwards suffered from retroflexion and chronic metritis, with general nerve prostration, a fibroid tumour being at length discovered in the posterior wall of the uterus.” (*Roehrig.*)

CASE 92.—*Uterine myoma following the use of a pessary.*—“A lady, aged 31 years, having borne a child had a prolonged lying-in.

She suffered great sorrow from the loss of her child, and being sterile consulted specialists, one of which applied Hodge's pessary, which she wore for two years. Having at length an excessive discharge from the vagina, the lady consulted Walther in Dresden. It was found that the pessary had caused, in the posterior half of the circumference of the uterus, a ring-like ulceration. The instrument was withdrawn and the injury was soon repaired, but two years after the patient returned with a fibromyoma at the same place as large as a goose's egg." (*Roehrig.*)

§ 30. *Tumours of the Vagina and Ovary.*

Cases of cancer of the vagina furnish facts of definite etiological import. In the cases observed by Dr. West the disease was limited to the anterior wall in only one case; in six cases it was limited to the posterior wall. "In the fungoid cases the posterior lip also was affected; in the epithelial the uterus was free, though in one instance the os uteri began to be red, spongy, abraded, and bleeding, yet I think not cancerous. In eleven cases, all of which were instances of fungoid disease, both vaginal walls were involved. In two, however, the anterior wall was affected. Summarizing all the cases, in six the uterus was perfectly healthy; in two it could not be reached; in two the affection of the uterus was slight, and its nature not quite certain; in nine it was the seat of decided cancerous disease."

"Only seven of the nineteen cases were observed between the ages of thirty-five and fifty; and the remaining twelve between the ages of fifty and sixty-six. Marriage and child-bearing apparently favour its production; for only one of the nineteen patients was unmarried; while the remaining eighteen had been pregnant ninety-five times, and had given birth to eighty-six children; or, in other words: there were 5·3 pregnancies and 4·7 labours at the full period to each marriage."*

Now if we make use of the explanation that has been offered of cancer of the neck of the womb, these data will at once

* West and Duncan: *Op. cit.* p. 632.

lose their obscurity. The factors of the two diseases are probably, in most cases, nearly the same. Sexual intercourse will rank as the leading cause. The mucous membrane of the vagina being unduly stimulated by contact with semen, the posterior wall will most frequently be the seat of the disease; and this explanation will account for the frequent association of vaginal cancer with cancer of the cervix; and in one affection as in the other the facts as to age, marriage, and child-bearing are closely similar. But in addition there are occasionally, in all probability, causes quite peculiar to vaginal cancer. I refer to mechanical frictions both in the act of coitus and in masturbation. In the latter way we are almost obliged to believe that cancer of the clitoris arises. In still other cases the irritation of unhealthy secretions, doubtless, plays a considerable part.

Gonorrhœal and venereal poisons and acrid uterine discharges are certainly concerned in the production of papilloma of the vagina. Papillomas "are found in their greatest luxuriance within and around the vulva of pregnant women affected with irritating discharges."* And what is most interesting from the standpoint of local causation in neoplasia, these papillomas generally disappear spontaneously after parturition.†

The interesting and important class of ovarian tumours are nearly all cystomata, a variety of neoplasm we decided at the outset to exclude from the present inquiry. The non-cystic tumours of this organ, as cancer, sarcoma, fibroma, &c., are so seldom met with that the facts in connection with them will hardly at present repay investigation, and therefore it will be well to pass on to more promising fields.

Cases Illustrative of the Facts Interpreted.

CASE 93.—*Epithelioma of the vulva succeeding a long-standing pruritus.*—"Mrs. D., aged 60, mother of three children. Men-

* Keyes: Surgical Diseases of the Genito-urinary Organs.

† Crocker: Diseases of the Skin.

struation ceased thirteen years since. Her health had always been good up to the time when present history begins. Ten years since the patient began to complain of itching of the vulva. This continued to be more or less troublesome, without materially interfering with her health, until about two years ago, when it became much more severe, depriving her of rest at night. During the past six months she has had more frequent attacks of the pruritus during the day, and at night has been obliged to obtain what rest she could by sitting up in an easy chair, as the itching became intolerable upon going to bed.

“She complains also of a soreness of the vulva, which she dates from an application made some months previously. The patient has been under treatment during the past two years without benefit. There was no history of leucorrhœa in the case. Upon examining the vulva, both outer and inner surfaces of the labia were found to be pale and glazed. The nymphæ were hypertrophied, and on the inner surface of the right one there was an ulcerated spot about one-third of an inch in diameter, which was covered with pale granulations. The membrane of cervix was of deeper colour than the vaginal membrane, and at the entrance to the cervical canal there was a very slight erosion. A small amount of thin yellow fluid escaped from the cervix. The itching was referred to the entire vulva, but more especially to the region of the clitoris and nymphæ. An examination of the urine for sugar gave normal results. The growth presented all the characters of a typical epithelioma.” (*Cushier: Medical Record, New York, 1879, vol. xvi. p. 440.*)

(The cause of the pruritus here is uncertain, but the case is valuable for the evidence it affords of long-continued irritation as an antecedent to epithelioma of the vulva. The neoplasm may safely be set down either to the condition which induced pruritus or to the means taken to relieve the latter. As showing the diversity of causative conditions even in cases of vaginal epithelioma, it may be mentioned that in one case the disease was attributed to injury from a badly adjusted strap attached to a hernial truss; and in another case to the fact that “the patient, during a long illness of her husband, had sat upon the hard edge of his bedstead, often for hours at a

time. At the point where pressure had thus been made upon the right labium and nates an epithelioma developed.”)

CASE 93.—“*Epithelioma propagated by contact from the posterior to the anterior wall of the vagina.*—This specimen was taken from the body of a woman, aged 34 years, who died in the Middlesex Hospital, under the care of Mr. Nunn, from a cancerous stricture of the rectum. The cancerous ulcer in the rectum has perforated the posterior wall of the vagina, forming a fistulous communication which will admit a goose-quill. On the anterior wall of the vagina, exactly opposite to the fistulous opening, is an inflamed circular patch, the size of a sixpenny-piece, superficially ulcerated and studded with little red granulations. This patch, when the vagina is collapsed, is in contact with the fistulous opening. The intervening mucous membrane of the vagina is normal. On microscopic examination of the reddened patch, numerous little deposits of cancer made up of concentric layers of epithelial scales are visible embedded in the mucous membrane. These correspond in every respect to the cancerous infiltration of the margin of the fistulous ulcer in the posterior wall.”

(If the vaginal epithelioma followed the irritation of secretions issuing through the fistulous opening, this case is a singularly neat illustration of the relation of cancer to locally incident actions.)

CASE 94.—“*Epithelial cancer of the labia at an early age.*—Patient aged 29. Appearance of fair health. She was a widow, the mother of several children, and strongly denied that since her husband died, about eighteen months, she had ever been exposed to the risk of venereal disease. The first symptom she had noticed was a violent itching about the parts, after which a crop of what she thought warts appeared. This was about eight months ago. When admitted, both labia and a considerable extent of the anus were involved in an ulcerated surface, covered with hard, irregular growths, and discharging a very offensive matter.” (*Lloyd: Medical Times and Gazette*, 1857, v. 1.)

CASE 95.—“*Epithelioma of the labia pudendi in a girl aged 20.*—A girl aged 20, strong and robust, had never been laid up for a day since infancy. . . . Occupying the upper half of the left labium

majus, and involving the adjacent portion of the labium minus, and just crossing the middle line above the urethra, was a very hard growth, made up of hypertrophied densely packed papillæ, with mushroom-like margins and indurated base. Under the microscope the growth presented the typical appearance of a squamous-cell epithelioma. The vaginal orifice was small and it was thought the hymen was still present." (*Arnott: Trans. Path. Soc. Lon.*, v. 24, p. 157.)

CASE 96. — "*Epithelioma of clitoris.*—Patient aged 61 years. Was married for 24 years and had been a widow for 14. She never had any children. She has always enjoyed excellent health. There is no family history of tumour. Three years ago two small tumours were removed from the left side of the vulva in the Chelmsford Infirmary. Lately she has been getting thinner. Its attachment exactly corresponds to the position of the clitoris, and the peduncle seems to be formed by the elongated body of the organ, the disease having commenced in a manner quite similar to that in which epithelioma usually manifests itself in the male organ." (*MacCormac: Trans. Path. Soc. Lon.*, v. 37, p. 357.)

(In each of these cases, doubtless, there were at work local actions which were not brought to light.)

§ 31. *Tumours of the Scrotum and Testicle.*

If, as I think, our hypothesis has shed much light upon the neoplasms just considered and in its turn has received strong substantiation this will be even more truly the case with the affection which must now engage our attention. Unlike cancer of other parts the causation of cancer of the scrotum is in no way confused. It has long been regarded as an unequivocal example of tumour-disease dependent on the action of external irritants. There can be no question that chimney-sweeper's cancer is the direct effect of contact with soot. The facts may be contemplated chiefly as they are given in Mr. Curling's "*Diseases of the Testis.*"

Here, fortunately, there may be observed the early stages of the neoplastic change, and it is interesting to note that the epithelioma begins as a papilloma. "It is generally developed

in the form of a small pimple, or warty excrescence, termed *soot-wart*, which often remains in the scrotum for months or even years, without undergoing any change. Usually there is only a single wart at the lower part of the scrotum; sometimes there are two or three of different sizes; and occasionally they are so numerous, and so abundantly and largely developed, as to form a considerable cauliflower excrescence.”* These warts are not in all cases confined to the scrotum, but may appear coincidentally upon the face or hands or the general surface of the body. Sir James Paget† thus speaks of the state of the skin in chimney-sweeps: “In many of them, even when they are thoroughly cleaned, the whole skin is dry, harsh, and dusky; and before operation for the removal of scrotal cancers in them it is a common question whether one or more warts or scaly patches near the chief disease should be removed with it. Such warts may exist in every part of the trunk and limbs; I have seen sweeps so thick-set with them that a hundred or more might have been counted.” It is Sir James Paget’s opinion that these warts are not at first malignant, and Mr. Curling says, “I entirely agree in the view taken by Paget that the soot-warts are not primarily cancerous. The cancer is the result of subsequent change. Some soot-warts never become cancerous at all.” The small excrescence in which cancer scroti usually originates is soft, vascular, and sensitive, and in many respects similar to the soft warts which occur on the internal membrane of the prepuce, and on the glans penis. The soot-wart appears, in fact, to consist of a congeries of morbidly enlarged papillæ. After a time the wart becomes soft, excoriated, and red, and exudes a thin, irritating discharge.” Thus, in the precancerous stage the soot-wart is almost certainly a true papilloma, and cancer beginning in this way exemplifies again the important truth that the higher neoplasms are generally the effects of slighter causes than those that produce cancer (p. 92), and that malignant tumours succeed the benign (p. 123). Papilloma is regarded

* Curling: Op. cit.

† Surgical Pathology.

by some pathologists as an instance of hypertrophy, and according to this idea the soot-wart precursory to soot-cancer corresponds to leucoma of the tongue or "erosion" of the cervix uteri.

How may the acknowledged cause of epithelioma of the scrotum be supposed to produce the disease? By irritation and exhaustion of the tissues; precisely as mechanical irritation will produce epithelioma of the lips, or ardent spirits epithelioma of the œsophagus. The skin of the scrotum is the usual seat of the disease not because of any special predisposition in its structural units, but because this part of the cutaneous surface is less frequently freed from the soot which lodges in its folds. The prepuce, the face, the hands, or other parts may be attacked. Mr. Curling quotes a case reported by Sir James Earle, of "a man who had a large sore resembling chimney-sweeper's cancer, which reached from the bend of the wrist to the knuckles, occupying almost the whole of the back of the left hand. The man was a gardener, and for several Springs had been in the habit of strewing soot on the ground round the young plants to preserve them from slugs. He carried the soot in an old garden-pot which hung on his left hand, while he strewed the soot with his right." Other cases have been observed among gardeners. Mention is also made of a female carrying on the business of a chimney-sweep who had a soot-wart upon her hand, and she had a son who presented a growth of the same nature upon his ear.

And not only may the disease appear elsewhere than on the scrotum, but irritants other than soot will produce scrotal epithelioma. Smelters, and those exposed to the vapours of naphthaline are sometimes afflicted. "In 1863, Mr. Hutchinson removed a cancer of the scrotum from a ship-caulker, a patient in the London Hospital, who had never been a sweep. In 1868, I excised, in the same hospital, an epithelioma the size of half-a-crown from the centre of the scrotum of a man aged seventy-two, a draper by trade, who had never been exposed in any way to contact with soot, and Sir William Ferguson

excised a similar growth from the scrotum of a man in King's College Hospital, who never came in contact with soot, but had worked much among guano for many years." (*Curling*.) But the fact remains, notwithstanding, that soot is the common cause. The disease is confined almost entirely to those countries where bituminous coal is used. In the United States and in France, where the use of anthracite coal prevails, it is perhaps never met with as chimney-sweeper's cancer; and in England the disease has become much less common with the introduction of machinery for sweeping chimneys, and, perhaps, greater attention on the part of sweeps to personal cleanliness. Or the reason may be of another kind. The present rarity of soot-cancer has been attributed by Mr. Lawson "to the fact that formerly soot fetched a high price, and was always sifted to free it from particles of mortar before it was sold. This sifting was hard work, and the motion of the body during the process caused considerable friction of the scrotum against the trousers, and this, combined with the irritation of the mixed soot and perspiration, seems to have been the determining cause of the growth of the cancer. Now that soot is of little value, it no longer pays to sift it, and consequently chimney-sweeper's cancer has almost disappeared."*

Observe that these multifarious phenomena cannot at all be reconciled by the assumption that the disease depends on the nature of the irritant, or in some peculiarity of the scrotal tissues. On the other hand the data are in complete agreement if we suppose that the intrinsic condition is a local exhaustion of tissue producible in any part by forces acting with sufficient strength for a sufficient time; and that this exhaustion ending in a reproductive process prepares contiguous tissues as soil for the growth of the new centres of development.

There are some facts to be considered relating to the ages of persons who have suffered from chimney-sweeper's cancer.

* Ericson : Science and Art of Surgery, 9th ed.

Generally the age is that observed in cancer of other organs ; “in the majority of cases which I have met with, the disease occurred between the ages of thirty and forty.” (*Curling.*) But, exceptionally, contact with soot will produce the disease at an early age. Cases have been reported at eight and fifteen years of age. Similar exceptions, as we have seen, occur in cancer of the rectum and uterus, and also in cancer of the ovaries. Thus we must infer that although maturity and old age are more favourable than youth yet if the exposure to soot and other conditions combine, the disease will appear early. Mature years presuppose the prolonged action of the special cause, and a ripening for changes which depend on declension of vital power.

Soot-cancer may ensue long after the cause has ceased to act. “It is known that persons who have been sweeps when young, but have abandoned the occupation, have afterwards been attacked with chimney-sweeper’s cancer, although they have long been removed from all contact with soot. A sailor, between forty and fifty years of age, was admitted into the London Hospital, with an ulcerated sore on the scrotum, presenting all the characters of genuine chimney-sweeper’s cancer. . . . He had been brought up as a sweep ; but for the last twenty-two years, during which period he had served at sea, he had not been employed amongst soot in any way whatever. The disease first appeared in the scrotum about three years before. In this instance, therefore, the influence of soot, if this were really the exciting cause of the disease, must have been exerted nineteen years before its appearance, during which long period the part was entirely exempt from the action of this substance. It has sometimes happened, after the morbid parts had been completely extirpated, and the wound healed, the patient having avoided further contact with soot, that the disease has reappeared, as it were afresh, a second and even a third time ; not, however, in the cicatrix of the wound, but in a different part of the scrotum.” (*Curling.*) The mystery of these facts may easily be penetrated. In the case spoken of the exposure in early life to the action of soot was not at that period of such

degree as to drain sufficiently the energies of the tissues, but the draughts then made when supplemented by the natural enfeeblement resulting from longer life proved the consummation of histogenic dissolution. And in like manner may be explained the fact that the disease may reappear in different parts of the scrotum.

There are recorded few particulars of the etiology of the benign tumours of the scrotum—lipoma, fibroma, &c. We may therefore pass them over and turn our attention to neoplasms of the testicle.

The usual form of cancer in the testicle is encephaloid, and its phenomena will constitute the staple of the remainder of the present section. Scirrhus, though known, is exceedingly rare.

Encephaloid is seen at a very early age, in mature life, and in old age. The age of greatest pregnancy is from twenty to forty years, as the following table* shows.

Before the age of 5	5 cases.
From 15 to 20	1 „
„ 20 to 30	11 „
„ 30 to 40	22 „
„ 40 to 50	6 „
„ 50 to 70	6 „
	51

Nothing, apparently, has been registered as to the influence of marriage. Nor are there facts immediately at hand showing whether the testicle of one side is more liable than that of the other. Sometimes, though rarely, both testicles are affected either simultaneously or successively. (*Curling.*) It is said that “there are few organs in which the origin of malignant growths can be so frequently and distinctly referred to some injury of the part as the testicle.” Many cases have been seen where

* *Curling* : *Op. cit.*

malignant disease has attacked an undescended testicle. Ten cases are referred to by Mr. Curling, including a notable one related by Dr. George Johnson.*

It is no longer disputed that the source of encephaloid cancer is the glandular epithelium. The secretory cells of the tubuli testis are in nearly all cases the elements among and from which the neoplasm begins to grow, though it has been known to start in the epididymis.† Often the tumour is a mixture of epithelial and sarcomatous cells, or it may be a true sarcoma. When sarcomatous it “almost always contains not only the chief varieties of sarcoma, but all the histoid formations which are met with in the sarcomata as well. Cartilage, mucous and adipose tissue, striped and unstriped muscle, enter more or less into the composition of sarcomata of this organ.”

It must be confessed that these slender data barely admit of induction, but such as they are our hypothesis is alone capable of giving them intelligibility. Setting aside those cases associated with obvious structural defect or injury to the testicle, over-use of the organs is probably the cause of cancer at the middle and late periods of life. In the absence of facts as to marriage and functional exercise, it is still legitimate to reason thus from what we have seen in cancer of the breast and uterus. The imperiousness of the sexual passion exposes the testicles as it exposes the breast and uterus to the risks of premature decline of vitality. We find that the morbid anatomy sustains this argument. The microscopic appearances demonstrate the destruction with cell-multiplication of the proper active substance of the glands, and as in other glands the tissue degeneration may extend to the connective frame-work and give rise to all the histoid elements of mesoblastic tissue. The disease is not essentially one of the serous and fibrous coverings of the testis, of the rete testis, of the epididymis, or of the vas deferens, but a disease of those elements which must

* Medical Lectures and Essays, p. 824.

† Cf. Birch-Hirschfeld: Arch. d. Heilkunde ix. p. 538

first feel the effects of excessive use. Such is, with extreme likelihood, the sole and efficient cause in the majority of cases, and in others it constitutes the foundation of the disease, injury and organic defect being supplementary causes. The remarkable frequency with which cancer has appeared in retained testicles supports these conjectures. This fact is indeed strong evidence of the truth of this reasoning and of the truth of the hypothesis of neoplasia at large. An undescended testicle is at a disadvantage, owing to its imperfect development, for the healthy discharge of its functions, and undoubtedly it is this disability which leads to its occasional partial dissolution by histogenesis. An undeveloped testicle is in the position of a mammary gland with its nipple retracted. Some may doubt whether a retained testicle is at any disadvantage whatever as a reproductive organ, and therefore it may be well to quote the remarks of Mr. Curling upon this point: "Hunter states that when one or both testicles remain through life in the belly, he believes that they are exceedingly imperfect, and probably incapable of performing their natural functions; and that this imperfection prevents the disposition for descent taking place. That they are more defective even than those which are late in passing to the scrotum, he infers from the circumstance that in quadrupeds the testicle that has reached the scrotum is considerably larger than the one which remains in the abdomen. . . . Professor Owen in commenting upon these observations states, "It seems remarkable that with this experience Mr. Hunter should have formed from inconclusive analogy, and promulgated, an opinion to occasion so much unhappiness as that which attributes exceeding imperfection and probable incapacity of performing their natural functions to testes which in the human subject are retained within the abdomen. That there is nothing in such a situation which necessarily tends to impair their efficiency is evident from the number of animals in which they constantly form part of the abdominal viscera; and in those in which the testes naturally pass into the scrotum, their continuance in the abdomen, according to our author's

own observation, is accompanied with a difference of size or shape ; now we may readily suppose that this may influence the quantity, but not necessarily the quality of the secretion." In the first edition of this work I expressed my adhesion to Owen's views, but subsequent investigations have led me entirely to change my opinion on this important point, and the facts which I shall adduce will be found to corroborate Hunter's opinion in a remarkable manner. When the testicle has not passed into the scrotum, the gland is nearly always small in size ; generally it is healthy but undeveloped ; that is to say, it has not undergone the enlargement and change in structure which takes place at puberty. In some instances, especially when seated in the inguinal canal, it is withered and atrophied, having suffered fibrous and more rarely fatty degeneration, and exhibiting no trace of glandular structure. In the second edition of this work I have detailed observations made by myself, Cloquet, Broca, Fallin, and Paletta, corresponding with this description, and I have since recorded several examinations which fully confirm its accuracy.

"Mr. Wilson mentions the case of a young man, twenty-five years of age, whose testicles never descended. He had some beard and not an unmanly appearance ; but although an imprudent, and in some things a dissipated person, he had never shown the least desire for women, or disposition for sexual intercourse. Similar cases have occurred in the practice of other surgeons. On the other hand, several cases have come under my notice, and there are others well authenticated, of cryptorchics, who, like Hunter's patient, had a masculine development, sexual desires, and powers of copulation. Nevertheless recent investigations show that a retained testicle only imperfectly executes its functions, and is rarely capable of forming healthy fertile semen." I have given these quotations at some length, because it is thus proved by facts of structure as well as of function that an undescended testicle supplies the necessary condition of histogenic dissolution. Either from the morbid and perverted action of its units, or

their inherent inability to bear the stimuli of natural function, an organ so circumstanced becomes the selected seat of encephaloid cancer.

Of the fact that the disease is occasionally seen in infants, at present only a speculative explanation can be ventured upon. Probably most, if not all, of these cases are determined by injury, and the disease finds a favourable predisposing condition in the tenderness and frailty of early childhood. There are many resemblances between the character of the viability of the tissues in infancy and that of the tissues in advanced life.

It remains to briefly refer to cystoma of the testicle. The interesting phenomena we met with in cystic disease of the mamma are almost exactly reproduced in the present instance. Retrogressive changes in the epithelium of the tubuli seminiferi or the rete testis, lead to epithelial accumulations, and the blocking and dilatation of tubes. As in the breast, the disease is accompanied by true neoplasia. The cystic decay renders the tissues suitable for the development of enchondroma, sarcoma, and carcinoma. "Enchondroma may be developed so abundantly as to encroach upon and obliterate the cysts, and to form the chief bulk of the tumour. Other morbid growths are also of frequent occurrence in cystic disease of the testicle. Myxoma or myxo-chondroma is not uncommon . . . The combination of malignant growths with cystic development is an element of considerable importance in this disease. I long ago pointed out, that after excision of a cystic testicle, while some patients remained well for years afterwards, others succumbed within two years from the development of malignant disease in the abdomen and other parts . . . It seems probable, indeed, that in some of these tumours the cystic structure prevails in the early stage, but at a later period the cysts become destroyed by the rapid growth of carcinomatous disease."* So often do the facts reiterate the truth that the root of tumour-disease is a deficiency and not an excess of vitality.

* Curling: Op. cit.

Cases Illustrative of the Facts Interpreted.

CASE 97.—*Cancer of an Undescended Testicle.*—"F. M. C., æt. 25, a pale, somewhat unhealthy-looking man, by occupation a shoemaker, married and without family, was sent to me on account of a large swelling situated in the left groin.

"He has been aware from early years that the testicle on the left side had not descended into the scrotum. He never suffered pain or inconvenience from this until about two years ago, when, after a hard day's work, he became sensible of a dull, heavy feeling in the part as it lay in the groin. Up to nine months since there was little change in the size of the testicle, but there was more pain in it. About this time he suffered a good deal from constipation, and strained violently at stool, and took large quantities of purgative medicines. He now observed that the testicle was getting larger. He states that he never sustained any injury to the part, and that he never suffered from syphilis. *Present Condition.*—The seat of the undescended testicle is occupied by an oval tumour, measuring five inches in length, and lying with its long axis in the inguinal canal. The integuments are wholly unchanged, and there are no enlarged glands. On uncovering the glans penis there are traces of venereal warts. Dr. Anderson, the Resident House Physician, reported that 'sections of the firm white part were found to consist of densely fibrous structure; and in the soft yellow spots numerous epithelial cells and amorphous matter were discovered.'" (*Pemberton: Illustrations of Various Forms of Cancer*, p. 63.)

(Perhaps the congenital weakness of the retained testicle may have been increased by the patient's occupation, or by injury in the act of coitus. (See case 100.) The state of the penis justifies a suspicion of incontinence.)

CASE 98.—*Cancer of the right Testicle associated with Inguinal Hernia of the same side.*—"Mr. D., æt. 43, a strong, vigorous-looking man, consulted me regarding his right testicle. Eight months since, without known cause, the right testicle began to enlarge. The enlargement was without pain. He never had a blow or strain, or suffered from syphilis. For the last six months has had pain in the lumbar region, and thinks he is thinner. The affected testis is large, heavy and ovoid in shape. The skin of the scrotum is free,

but its wrinkles are gone, and numerous enlarged veins traverse the surface of the tumour. There are no diseased glands to be detected. On the same side there is an inguinal hernia, readily reducible, and for which a truss is constantly worn. He died by the gradual progress of the disease on August 28th in the same year.” (*Pemberton.*)

(In this case, possibly, a contributory condition of the disease was some interference with the health of the right testicle, occasioned by the pressure of the hernial truss upon the structures contained in the spermatic cord.)

CASE 99.—*Cancer of the Testicle after Injury.*—“E. T., æt. 36, married, a butler in a gentleman’s service—a short vigorous man—was admitted on account of an enlargement of the left testicle. Eight months since, whilst riding on horseback, he bruised the left testicle severely against the pommel of the saddle. The immediate effects of the injury were such as to require leeches and fomentations; but he did not keep quiet long enough to get quite well—a marked increase in the size of the part remaining when he resumed his occupation. He died with marked symptoms of the internal development of encephaloid cancer.” (*Pemberton.*)

(In cancer of the breast and other parts, we have seen again and again how the life-conditions of a particular structure or organ fit its units for neoplasia on the advent of acute injury. The phenomenon is rehearsed in the present case. We may suppose that functional exercise was the predisposing and violence the determining factor.)

CASE 100.—*Cancer of an injured retained testicle.*—“In December, 1871, I was consulted by a gentleman, aged 35, a married man, apparently in good health. His surgeon, Mr. Lawrence, of Bath, stated in a letter that about three years ago his attention was called to the patient’s right testicle, which was lodged in the inguinal canal, but presented at the outer ring About three months since, after being compressed in coition, the testicle became acutely inflamed. This soon yielded to leeching, fomentation, and rest. About a week ago a similar attack, but less acute, occurred after more active exertion than usual. On examination,

I found an oval swelling, the size of the closed fist, lying obliquely in the right groin, and covering the outer ring It was impossible to determine precisely the nature of the swelling, but I strongly suspected that it was a serious organic enlargement of the testicle, and therefore recommended its removal by operation. This was done a few days after, when the disease proved to be malignant disease." (*Curling.*)

CASE 101. — *Recurrent fibroid affecting a retained testicle.* — "A man, 39 years of age, married, but without children, was admitted into the Hotel Dieu, at Lyons, for a tumour in the right groin, which had been enlarging for seven or eight years, and had increased rapidly the last four months. It was excised, and proved to be a fibro-plastic growth affecting both the testicle and epididymis." (*Haraud, quoted by Curling.*)

§ 32. *Tumours of the Penis.*

The remaining tumours of the sexual system of the male are, in the main, penile. Epithelioma, though not common, is the most important, and numerous facts have been observed bearing upon its etiology. In all cases, probably, it first appears at the end of the organ. "It always commences in the anterior extremity of the penis, affecting the body of the organ only by extension from the original starting-point."* The usual position is the sulcus behind the glans; next on the reflected layer of the prepuce and on the glans itself.†

It is rare before the age of forty-five, and is chiefly met with between forty-five and seventy.‡

Congenital phimosis is given an important place among the actual causes. Syphilis may also be concerned in producing the disease—"in the production of warts, by leading to the formation of chancres and by the scar of a chancre." (*Pemberton.*) "The degeneration of long-standing venereal sores has, in some

* Ericson : Science and Art of Surgery.

† Pemberton : Clinical Illustrations of Various Forms of Cancer.

‡ Holmes and Hulke : System of Surgery.

instances, established it, and I have seen it myself follow the effects of direct external violence.” (*Pemberton*.) “Quite a different way in which epithelioma may occasionally invade the penis is by starting in the irritation of an urinary fistula.”*

These statements concerning the direct causes agree with the observed seats of the disease. The anterior extremity is, perhaps without exception, the part that suffers first from epithelioma, and this is the part affected by phimosis and syphilis. Phimosis is supposed to induce the disease by causing the retention under the foreskin of decomposed and irritant secretions. Now such secretions are likely to accumulate behind the corona of the glans and upon the reflected portion of the prepuce.

A causal relation between epithelioma and venereal disease appears to be unquestionable. As in the tongue, it may arise from the degeneration of syphilitic scars or may grow out of the active tissue changes set up by the venereal poison.

By means similar to the foregoing, epithelioma may be generated in urinary fistulæ, the general condition being chronic irritation.

In addition to these recognized causes, there are probably others equally important but unrecognized. Excessive use of the penis will undoubtedly tend to produce the tissue changes which lead to neoplasia. Mere friction, if it be immoderate, of the epithelium of the glans, must sometimes, alone or combined with other factors, prove effective. And unhealthy vaginal secretions, other than those associated with gonorrhœa and syphilis, may occasionally be part causes of the disease.

Thus the known and assumed causes of epithelioma of the penis are of many kinds, and it adds greatly to the strength of our hypothesis that it enables us to comprehend the *modus operandi* of factors so various. The influence of phimosis, of syphilis, stricture, urinary fistulæ, noxious vaginal secretions,

* Holmes and Hulke: *Op. cit.*

injury or friction from inordinate sexual intercourse, can all be conceived to set up the hypothetical conditions of tumour-disease.

Epithelioma is almost the only known form of malignant disease affecting the penis; yet it appears that sarcoma or medullary carcinoma may, as elsewhere in the body, be occasioned by injury. (See appended cases.)

As to the rest of the tumours of the penis it may be noticed that the common papilloma is met with in the same situations as epithelioma, that its causes are of similar nature, and that it often precedes the appearance of epithelioma. Papillomas “are caused by the contact of irritating fluids . . . or simply by lack of cleanliness. The most favourable conditions for their production consequently exist in gonorrhœa, balanitis, or when mucous patches occupy the cavity of the prepuce. Their favourite seat is just behind the corona glandis, but they are also encountered anywhere within the cavity of the prepuce—at its orifice, upon its surface, or even within the urethra.”*

Cases Illustrative of the Facts Interpreted.

CASE 102.—*Cancer of the penis associated with congenital phimosis.*—“J. H., æt. 14, was brought to me about three years ago; and the history given me at that time was that, a few months after birth, a brother practitioner was requested to see him, for what, I presume, from the father’s description, was congenital phimosis. He never could pass urine freely; in the act of micturition the prepuce would bulge out. This took to growing, and when he presented himself to me he had an excrescence, very like a glans penis, through which he passed water, as from the rose of a watering-can. *Actual Condition.*—A stupid, ill-developed boy, but not unhealthy in look. The penis is twisted and thickened, and occupied in most of its body by closely-packed healthy-looking granulations. The glans is distinct and only partly affected by similar ulcerations. I subsequently learned from Mr. Mason that he died from the effects of exhaustion, December 20th, 1866.” (*Pemberton.*)

* Keys: Surgical Diseases of the Genito-urinary Organs.

CASE 103.—*Epithelioma of the Penis associated with Syphilis.*—"A gentleman, æt. 69, died of epithelioma of the penis, September 3rd, 1865. When 35 years old he had a chancre, which healed up under mercury, but left a scar, which was visible for some time after. Seven years before his death he noticed some redness in the locality of the scar. This redness subsequently became a sore surface, which extended from time to time and then healed up. . . . It was not till a year before he died that any induration was observed beneath the sore. At first this was very limited, but by degrees half the glans penis became hard and solid." (*Sibley, quoted by Holmes and Hulke.*)

CASE 104.—"Some years ago, a milkman consulted me on account of an offensive discharge which issued from beneath the foreskin, which was phimosed, inflamed, œdematous and indurated in the region of the cervix. There were small hard buboes in both groins, and there was a history of excessive illicit connexion The foreskin being thus laid open, the appearances were very much what was anticipated: a good deal of pent-up, offensive secretion was removed with pledgets of cotton-wool, from a partly warty and partly ulcerated mass adherent to the corona glandis, cervix and the prepuce Under the use of antiseptics the penis assumed a healthier condition in a few days, but then a rose-rash appeared on the chest, and there were other signs of secondary syphilis. Under antisyphilitic remedies, the lesion on the penis did not entirely heal. Of course the œdema of the prepuce had subsided, but the growth and ulceration in the region of the corona reappeared. The diagnosis was now unmistakable; the case was one of syphilis and epithelioma co-existing." (*Jennings.*)

CASE 105.—*Cancer originating in a Urethral Stricture (?)*.—"The patient, a man æt. 55, was admitted for supposed stricture. It proved to be a primary carcinoma of the urethra, a fungating ulcer, two and a half inches in length, being found in the floor of the urethra, with rounded masses growing into the substance of the penis. Some of the lumbar glands contained cancer." (*Holmes and Hulke.*)

CASE 106.—*Epithelioma of the Penis following Injury.*—"Mr. F., a farmer, was out shooting; and while he was trying to force his way through a hedge, a thorn penetrated his trousers and wounded

his prepuce, causing blood to flow. He took little heed of it at the time; but a few days later, feeling some heat and uneasiness, he found swelling and irritation about the wound. This rapidly increased, and he then consulted his medical man, who advised certain remedies. The penis grew worse, and the whole glans presented a mass of carbuncular hardness in a short time, and was very painful. An incision into it gave no relief, and suspicion being confirmed on consultation, the penis was amputated, and the growth proved to be an epithelioma. This was only a few weeks from the date of injury." (*Walker: British Medical Journal*, 1882, i. 459.)

(What were the conditions which made it possible for an injury to set up neoplasia in this case? Probably a feebleness of tissue resulting from the actions of the part throughout the life of the individual, and a feebleness consequent on the distance of the part from the centre of blood-supply. Mr. Pemberton has recorded a similar case. "J. T., æt. 67, whilst getting in a load of coals, happened to fall, and in doing so violently bruised the glans penis. A sore formed at the seat of injury, and gradually spread, destroying the parts before it.")

CASE 107.—*Sarcoma (?) of the Body of the Penis following Injury.*—"C. C., æt. 18, native of New York, was admitted into St. Luke's Hospital, February 11th, 1869, with an enlargement of the penis, which he said had existed four months. At that time being in good health, he slipped while ascending a ladder, and fell in such a manner as to catch the penis between one of the rounds and the pubes. The blow was severe enough to produce an ecchymosis on the under surface of the organ, about an inch from the scrotal junction, together with severe swelling and soreness of the injured parts. From that time the swelling steadily increased, the penis becoming tense and continuously erect. *Condition on admission.*—The penis was much enlarged, knobbed, and permanently erect. The skin was normal, though somewhat thinned and freely movable in the subjacent parts. The growth did not extend beyond the root of the penis, and was apparently confined to the corpora cavernosa, which were generally tense and elastic, bulging in places where it was evident that thinning or giving way of the sheath

had taken place. The glands in the right groin were enlarged. The extent of the enlargement of the penis was rendered yet more striking by the comparatively undeveloped state of the rest of the genital organs. The testicles were about the size of small marbles, and not a sign of hair was to be seen on the pubes. His stature was small, face puny and physique slight. . . . The increase of the tumefaction of the penis and of the inguinal glands was steadily progressive. His relatives, on learning the nature of his disease, decided to remove him to his home, some thirty-five miles distant from the city, whither he went March 22nd, to die some seven months later." (*Weir: American Journal of the Medical Sciences*, April, 1876.)

(In trying to divine the conditions of which this tumour was the sum, regard should be given, it would seem, to the imperfect development of the sexual system. The testicles were very small, and there was little hair upon the pubes. The disease probably originated out of the conjunction of this condition and the accident. The organ injured being congenitally weak, the injury would effect such local but extensive reduction of vital power with liberation of new centres, that the latter easily gained the upper hand in the competition for nourishment.)

§ 33. *Recapitulation and Conclusion.*

Tumours of the alimentary canal exhibited to us a marked relation to the direct action of the environment, but in the organs of the sexual system tumour-genesis is less immediately under the sovereignty of external conditions. The agencies at work as causes are mainly physiological stimuli connected only indirectly with the environment. Though we found that inflammation, traumutic injury, mechanical pressures, and chemical irritants are common accessory causes, and sometimes the essential causes, of cancer and other tumours, yet it clearly appeared that functional excitations proceeding from within the organism and involving a waste of tissue-energy are, in the etiological sense, the groundwork of neoplastic changes in the organs of the sexual system. This was seen to be specially

the case with tumours of the breast, uterine myoma, and encephaloid of the testicle. Even here, however, neoplasia must in the last resort be referred to the external world; for the catamenial rhythms, sexual excitement, child-bearing, &c., are not independent of the relations of the organism to its surroundings.

The present chapter has helped materially to strengthen some former conclusions. The tumours of each part are seen again to be local by parentage and by causes. And again the causes are shown to be special for each organ, special in nature and special in co-operation; and every case is more or less distinctive.

Some of the relationships dogmatically given in Chapters III and IV, of the benign to the malignant tumours, have in the present chapter found inductive confirmation. The benign tumours of the breast and uterus are undoubtedly expressive of katabolic changes less profound than obtains in cancer. The causes are slighter and less persistent, and the tumours tend to appear before the general vigour of the organism has begun to decline.

Looking at the results of this chapter as they affect the general hypothesis of tumour-disease, we must now acknowledge that its reach and explicative power are such as entitle it to most favourable countenance. To make fairly clear and amenable—not to overstate the services of the hypothesis—phenomena so dark and intractable as those we have just been engaged with, is a considerable achievement.

CHAPTER VI.

THE SPECIAL CONDITIONS OF TUMOUR-DISEASE *concluded.*

Tumours of the Cutaneous System—Tumours of the Osseous System—Recapitulation and Conclusion.

§ 34. *Tumours of the Cutaneous System.*

The skin is the common seat of epithelioma, and some of the conditions special to the development of epithelioma in this structure afford remarkable proofs of its origin by histogenic dissolution. We saw in cancer of the lips and scrotum how the disease there is related in the most direct manner to injurious external actions. A like relationship obtains in other parts of the integument. Skin-cancer very frequently begins in the cicatrices of wounds and burns. The liability of scar-tissue to epithelioma has long been noticed, and in the Hunterian Museum there are many specimens testifying to the fact. As cases of this kind are of great value in our present inquiry, it will be well to glance at a few of them.

CASE 108.—Specimen No. 474, Hunterian Museum, is the lower part of the right leg from a man aged 50, with a large epithelial cancer on its front and sides. “Eleven years before the amputation of the limb he received a blow on the shin, and thickening of the bone followed. For the last two years he was laid up with a large spreading ulcer.”

CASE 109.—Specimen No. 475, Hunterian Museum, is “a right foot presenting on the outer side of the ankle an epithelial cancer occurring in a large cicatrix, the result of a severe injury received twenty years before.”

CASE 110.—Specimen No. 478, Hunterian Museum, is “a right elbow-joint with all the neighbouring structures, showing epithelial cancerous ulceration of the integuments in the cicatrix of a burn.

From a man fifty years old. The disease formed in the cicatrix of a burn which occurred when he was about seven years of age."

The following cases reported by Mr. Pemberton* show how cancer may be aroused in cicatrices by their repeated injury:—

CASE 111.—"J. P., æt. 64, a vigorous looking old man. Fifty-two years since he was severely burned on the neck and anterior aspects of the right arm and forearm. After a long time the wounds healed soundly, leaving an abundant scar from the arm to the forearm. . . . About three years ago the injured limb was severely crushed between two carts, but no external wound was made. Having recovered from the effects of this accident, the cicatrix on the forearm broke into a sore, and slowly increased until it extended over a space measuring five or six inches in circumference."

CASE 112.—"G. S., æt. 58, a labourer, was admitted on account of a long-standing ulcer situated at the upper part of the right leg. For ten or fifteen years he has had a sore at the upper part of the leg. This came at first from a blow, and healed many times; but, being out at work chiefly in the night time, he repeatedly injured the same part again."

The frequency with which cancer forms in the cicatrices of operation wounds is only two well-known, but there is a fact in connection with scar-tissue neoplasms that is not explained by the current doctrine of recurrence. I refer to the cancerous nodules found in the tracks of sutures after operations for carcinoma. Here it is most probable that histogenic dissolution is set up in the cells of the scar-tissue by the reducing action of the sutures.

The cause of epithelioma of the skin as the disease is seen among the native Kashmiri poor at Sirinagar well deserves our attention. "The disease as it occurs in that locality, shows a remarkable preference for the abdomen and inner aspects of the thighs. It invariably occupied these sites in the thirty patients. Dr. Elmslie attributed the disease to the universal

* Clinical Illustrations of various forms of Cancer, &c.

employment, in cold weather, of the *Krangri*, an earthenware pot usually covered with fine wicker-work, containing ignited charcoal, which is worn under a loose woollen gown in close proximity to the skin. Indoors or in the sitting posture, the *Krangri* is placed between the thighs.”* Epithelioma is also met with in the Hebrides among people exposed to peat-smoke.

Now these illustrations, which might easily be indefinitely multiplied, exhibit just those conditions of neoplasia recognized by our hypothesis. Scar-tissue, as previously stated, shows in several ways that its vitality is less than the structures it replaces; then the scar-tissue, in these and other instances, is old; it often happens that not only is the subject advanced in life, but the cicatrix is one of long-standing, the injury it repairs having been inflicted early in life. Next is the very noteworthy fact that the scar-tissue has itself been repeatedly injured. Mr. Pemberton has remarked that “repeated injuries in the situation of a former wound, and above all the persistence over many years of an ulcerated surface of considerable extent, are causes that appear directly to excite the production of cancer.” Of this group of facts there is but one interpretation, namely, that the new growth is the consequence of local exhaustion of vitality.

Another class of cases whose import is in no way different are the cases of epithelioma and sarcoma originating from warts and moles. In thirty-four cases of melanosis, fifteen developed in or near a congenital mole, wart, or mark.† It will be seen from the details subjoined that sometimes injury of the congenital growth precedes the appearance of the cancer.

CASE 113.—“H. W. J., æt. 23, single, a cooper by trade, was admitted with a coloured warty growth upon the integuments covering the lumbar portion of the spine. About two years since he discovered by chance the presence of a wart, about the size of his finger

* Norman Chevers: *Medical Times and Gazette*, 1884, v. 2, p. 399.

† Pemberton: *Op. cit.*

nail, in the hollow of his back, which had, no doubt, been there from birth. It was at that time free from pain; but in the course of a few months, some irritation having been recognized by the friction of his apron strings, it discharged and became a source of annoying itching. As it increased it was removed and treated with caustics. Subsequently it gave rise to fatal melanosis." (*Pemberton.*)

CASE 114.—"P. C., aged 53, a collier, married—a worn, pale-complexioned man—was admitted having a black patch of diseased structure on the right cheek. He had always, within his recollection, a mole in this situation. It never occasioned him pain or annoyance until within three months of his admission. The first occasion of its doing so was after it had been accidentally wounded by a barber in shaving. After this it began to prick and shoot, and to increase slowly in dimensions. . . . Though of delicate constitution, he had followed a laborious employment in the pits, and had encountered the hardships and accidents incidental to his occupation. . . . On the 10th of April, sixteen days after admission he died suddenly." Examination after death disclosed general melanosis of internal organs. (*Pemberton.*)

CASE 115.—"J. L., æt. 54, single, a brewer by occupation and of intemperate habits, was admitted on account of long-standing ulceration of the right hand. The disease had been growing for two years, having originated in a wart that had been present from his birth, near to the metacarpo-phalangeal articulation of the index finger on the back of his hand. This he injured by contusion several times, so that at length a permanent sore became established." (*Pemberton.*)

The proclivity to form tumours shown by congenital moles and warts is exactly parallel to the same proclivity of scar tissue and vestigial structures. Moles and soft warts consist of epithelial and sarcomatous cells grouped much as they would be grouped in a cellular tumour. It is probable that these redundant growths are foetal remains, and being crude functionless bodies their conditions of life must be favourable to those reduction-changes of which histogenic dissolution is the consequence, and especially if there be the provocation

of injury. Nævi, also congenital tumours, have been known to undergo the transformations of neoplasia.

There remain other noteworthy facts as to the causes of epithelioma of the skin. The navel is sometimes the seat of cancer, and the probable reason is that besides containing cicatricial tissue, the navel, in the uncleanly, forms a nidus for the lodgment of irritating matters. Thus, a growth in the umbilicus was found on removal to have been caused by a collection of hard and inspissated sebaceous material the size of a cherry stone.* Malignant disease may also be connected with umbilical hernia.

Sometimes epithelioma will start from sebaceous tumours in the areola of the nipple (*Bryant*) and in the scalp, showing again how damaged and degenerate parts supply suitable conditions for neoplasia. The following case is an illustration.

CASE 113.—“A man, aged 55, with a wen on the vertex, which had existed for a score of years or more, accidentally struck it against a sharp piece of wood. Inflammation of the tumour followed, then ulceration and sloughing, which was followed, after a few weeks, by cancerous disease of the entire border and even base of the ulcer.”†

Similarly, cancer of the skin succeeds lupus, either growing from its scars or by an unbroken continuity of disintegrative changes. Probably the melanotic whitlow of Hutchinson is an example of malignant disease supervening upon and produced by chronic inflammation. It begins as a chronic onychitis and gradually runs on into a fungating growth.

It is now admitted that rodent ulcer must be included among the epithelial neoplasms of the skin. Unlike ordinary epithelioma, which originates from surface epithelium, the disease under consideration is in all likelihood a disease of the cutaneous appendages, as the sebaceous glands (*Thiersch*, *Butlin*), sweat glands (*Thin*), or hair follicles (*Hume*).‡ Of

* Foulerton: *Illustrated Medical News*, vol. ii. 1889.

† Lewis: *New York Medical Record*, vol. ii. 1889.

‡ Crocker: *Diseases of the Skin*.

its causes but little is known that is beyond dispute. It is a disease of advanced life and in numerous cases has undoubtedly been determined by injury. Possibly it is connected with some state of the system which unduly excites the glands of that part of the cutaneous surface most liable to attack—the upper two-thirds of the face. Alcohol, as we know, may profoundly modify the skin of the face, and the connection of tumours of the skin with irritations coming from within the body is shown by the frequent association of sarcoma and diabetes.

Alibert's keloid partakes of some of the characters of malignant growths, and if it be regarded as a true autonomous neoplasm we should note that it may appear "at the site of leech bites, acne scars, scars from herpes, and all kinds of pustular and vesicular eruptions, and even from contusions, frictions, or blisters in which there is no cicatrix." (*Crocker.*)

The benign tumours of the skin are in most cases of apparently spontaneous origin, so unobtrusive are their causes, but they are also not seldom attributable to obvious causes. The verruca vulgaris occurs on exposed parts, as the backs of the hands and the face, and is often due to contact with noxious matters, instance the warts that come from handling the cadaver. Then moist warts are found in the axillæ, under the mammæ where they overhang, and in the umbilicus, all places favourable for the accumulation and decomposition of secretions. Finally, there is the lipoma of the skin at the site of pressure from braces, or weights carried on the shoulders and hips. A fatty tumour grew on the ilium of a laundress at the spot where rested a linen-basket she was in the habit of carrying.

Further Cases Illustrative of the Facts Interpreted.

CASE 117.—*Epithelioma of the face and scalp.*—Specimen No. 485, Hunterian Museum, is "the left side of the face of a woman aged 60, showing a large mass of epithelial cancer surrounding and involving the eyelid, extending inwards over the bridge of the

nose, and downwards to within an inch of the lips. . . . Close above the ulcer on the face is a more recent epithelial growth on the scalp; this has perforated the bone and invaded the dura mater. The patient was a hawker, and accustomed to carry heavy basketfuls of fruit on her head. For three years she had observed a small spot, like a mole, on the hair-line on the left side of the forehead. Six months before death it began to grow rapidly, and then to bleed freely."

(Dirt and friction incidental to the occupation of the patient probably assisted in the causation of the neoplasm in this case.)

CASE 118.—*Epithelioma of the face following injury*.—The patient "was injured several years ago by a splinter of hot iron striking the bridge of the nose, and which, glancing to the right, ploughed its way nearly to the internal canthus. It healed pretty promptly, but had always been a little tender near the eye. For a few months past it has been more troublesome, and when he presented himself at the clinic a well-marked epithelioma had developed in that portion of the cicatrix nearest the angle of the eye." (Lewis.)

CASE 119.—*Epithelioma of the thumb beginning as a wart*.—"A young man of dark complexion, short stature, and fine *physique*, aged 21, was admitted into University College Hospital. He had been employed at a skin and leather warehouse, had always lived well, had enjoyed good health, and had never had syphilis. About six years previously the patient had noticed a small wart on the back of the phalangeal joint of the left thumb; it bled occasionally when rubbed, and grew slowly larger, but did not trouble him for four years. It then began to spread rapidly towards the nail and round the outer side of the distal phalanx. He then came to the hospital, and the growth was apparently destroyed with caustic. After a few months, however, it reappeared, and soon extended further than before. In February, 1874, nitric acid was again applied, but ineffectually; for on the readmission of the patient eleven months afterwards, nearly the whole of the distal phalanx of the thumb was covered by a nodular growth with a sloughy ulcerated surface." (Erichsen.)

(This case is a good illustration of the fact that with slight injury to the tissues, and at an early age, the resulting neoplasm is likely to be fully developed and benign, and only becomes immature and malignant as the actions hurtful to the tissues are multiplied. The handling of skins and leather was probably the essential cause, first of the papilloma and then of the epithelioma.)

CASE 120.—*Sarcoma-cutis of the foot*.—"A woman, aged 40, admitted under the care of Mr. Willett, stated that she was quite healthy a year previously to her admission. At that time, after a walk in a new pair of boots, she noticed a blood-blister (of the size of a sixpence) on the sole of her right foot. She was very certain that, previously to the blister, her foot was sound. After a while the blister broke, leaving a raw surface, which never healed, and gradually increased in size. On admission in the hospital, a growth (the size of a florin) was seen on the foot, in the site of the blister. It was moderately hard, and covered with a thin bluish cuticle. The growth was removed, with a narrow margin of healthy skin round it, and a flap of skin, cut on the near side of the foot, was turned downward, so as to cover the wound on the sole. The wound healed satisfactorily, and the patient was discharged from the hospital in fair health; there was, however, a slight enlargement of one of the femoral glands. In six months she was readmitted. At the margins of the cicatrix on the foot were several little nodules of recurrent disease; but the portion of skin brought down to cover the wound was healthy. In the groin the femoral glands formed a mass of disease of the size of a small orange, and about the upper part of the body were a few small subcutaneous nodules. She was greatly emaciated. During the next few weeks hundreds of small nodules appeared beneath the skin of the trunk, the limbs remaining free. Symptoms of internal complication rapidly supervened, and she died nine months after the original operation." (*Cripps : British Medical Journal*, 1882, vol. i. p. 653.)

(The common site of sarcoma-cutis is the sole of the foot, especially the under surface of the heel. The principal conditions deciding the frequency of the disease in this situation

are undoubtedly the great liability of the parts to injury, and its remoteness from the central source of nutriment.)

§ 35. *Tumours of the Osseous System.*

Tumours of the osseous system chiefly acquire their importance from the frequency with which the bones are attacked by sarcoma. Pathologists are now almost unanimously of the opinion that sarcoma is the only primary malignant growth occurring in bones, and that carcinoma is probably in all cases either of metastatic origin or due to local extension from contiguous or neighbouring tissues. Our consideration then of malignant tumours of bone resolves itself into a consideration of sarcomatous tumours.

Distinguished by their histological characters these new growths are divided into the round-celled, spindle-celled, and myeloid varieties; and distinguished by their origin from different elements of osseous tissue they are divided into central sarcomas and periosteal sarcomas. By central sarcoma is meant one starting from within the substance of a bone and by periosteal sarcoma one starting from the periosteum or periosteal surface of bone. Periosteal sarcomas may be subperiosteal or parosteal.

In connection with the conditions of their development we may first note some facts as to the relative frequency with which sarcoma occurs in the different bones of the body. Although it has been met with in nearly every part of the osseous system, yet practically the disease has a limited distribution and mostly affects the long bones. The femur, tibia, humerus, and radius and ulna, are those most liable to suffer. It is also seen very frequently in the face but only occasionally in the calvarium, scapula, clavicle, pelvis and foot. The ribs, sternum, spine, and bones of the hand, are rarely attacked.

We next find differences of liability among the bones usually affected. The disease is seen many more times in the lower than in the upper extremity. Out of 165 cases collected by

Dr. Gross* the long bones of the leg were the seat in 76 per cent., as the following table shows :—

Femur	67 instances.
Tibia	46 „
Humerus	25 „
Fibula	13 „
Ulna	7 „
Radius	6 „
Ulna and Radius	1 „
	165 „

And these observations are fully confirmed.

Besides this greater predilection of the lower extremity as compared with the upper we next discover that the individual bones of the two extremities are not all equally subject. In the lower limbs the femur probably stands first, then the tibia, and lastly the fibula; and in the upper limbs the humerus is affected perhaps twice as often as the ulna and radius put together.

Not less remarkable than these facts is the tendency shown by sarcoma to begin in particular portions of the long bones. Thus, the lower epiphysis of the femur and upper epiphyses in the tibia and fibula are by far the most frequent seats; but in the humerus it is the upper epiphysis, and in the radius and ulna the lower epiphyses that generally succumb. This is seen from the tabulation of seventy examples of central giant-celled or myeloid sarcoma.†

Tibia, upper epiphysis	in 21 cases,	lower epiph.	in 2 cases
Femur „ „ „	2 „ „ „	17 „	
Fibula „ „ „	7 „ „ „	3 „	
Humerus „ „ „	5 „ „ „	1 „	
Radius „ „ „		5 „	
Ulna „ „ „	1 „ „ „	3 „	
Femur shaft	2		
Humerus „	1		
Radius „	1		

* *American Journal of the Medical Sciences*, July, 1879.

† Gross: loc. cit.

It is noted of six out of twelve cases of myeloid sarcoma that the shaft ended abruptly in the soft matter of the tumour,* which definitely proves the epiphysis to have been the seat of origin.

Of the periosteal or peripheral sarcomas, those in the table being central, a much larger proportion occur upon the shaft, a majority indeed in the case of the humerus. Nevertheless, in the periosteal tumours there is a tendency to affect the same epiphyses. Speaking of periosteal tumours of the femur, Mr. Butlin observes† that “most of the spindle-celled, like the round-celled, tumours affected the lower portion of the bone; indeed only one of them was of the upper third.” Again, “like the tibia, the fibula is most often affected at the upper end; indeed each one of these three tumours grew about the upper end or upper third.”

Of the remaining bones in which sarcoma is seen, we find in the face that the favourite seats are the jaws, and most frequently the upper jaw. The clavicle is oftenest affected at its acromial end. “They exhibit a preference for the body or outer extremity of the bone.”‡ In the pelvis the innominate bones are usually attacked, and in the foot they may begin in the tarsus or metatarsus. The calvarium is the common seat in the skull.

Osteo-sarcoma is a disease of youth and early manhood. In 147 cases§ of central myeloid sarcoma there were

45 between 10 and 20 years of age.

55	„	20	„	30	„	„
26	„	30	„	40	„	„
11	„	40	„	50	„	„
7	„	50	„	60	„	„
3	„	60	„	70	„	„

In periosteal growths the age of greatest liability is probably

* Wilks : Guy's Hospital Reports, 3rd series, vol. 3, 1857.

† Sarcoma and Carcinoma.

‡ Jones : Diseases of the Bones.

§ Gross : loc. cit.

somewhat less than in central growths. "Speaking in very general terms, central tumours occur in persons older than those who are the subjects of sub-periosteal tumours; for while the latter not uncommonly attack young subjects, or even children, the former are by no means rare in persons advanced in years."*

As to the influence of sex, there is a sensible preponderance of males among the subjects of both central and peripheral sarcomas. Males are more liable to the occurrence of myeloid tumours by 17 per cent. than females (*Gross*). Of Mr. Butlin's cases of sub-periosteal tumours, fifty-three of the subjects were males and twenty-seven females.

Traumatism is a more pronounced factor in the production of osteo-sarcoma than with any other class of neoplasms. "A very large majority of the sarcomata of bone are traced by the patients to some definite injury, such as a blow, a kick, or a fall."† The cases of central myeloid tumours collected by Gross show that "traumatism was the assignable cause in nearly one half of the 144 cases in which etiology is recorded. They could be traced to blows, falls, kicks, sprains, fractures, and other injuries." And in the round-celled periosteal sarcomas 54 per cent. were traceable to traumatism.

These are the conditions of osteo-sarcoma which observation has thus far securely established, and we may now try to effect a synthesis of them. Why does sarcoma attack by preference the bones of the limbs? There has to be explained the rarity of the disease in certain bones and its frequency in others. If we survey the functions and life-conditions of the several parts of the skeleton, the bones which sarcoma most affects are seen to be those called upon to discharge the largest share of functional service. The offices of the skeleton are to give shape to the body by supplying a firm and resisting

* Butlin: Op. cit.

† Heath: Dictionary of Surgery.

structure, and, as in the calvarium, ribs, and vertebræ, a hard casing to protect vital and vulnerable parts. It also furnishes surfaces for the attachments of the apparatus concerned in effecting movements. Now, if we consider the predilection of sarcoma for certain bones, the fact is obtruded upon us that parts most subjected to functional actions are in the highest degree subject to the disease. Setting aside sarcoma of the jaws, which we shall deal with presently, it may be noticed that in about three-fourths of the cases the disease affects the lower limbs. The lower limbs are active above all other members. Besides serving as locomotor organs, these parts have to bear in large measure the strains necessitated by maintenance of the erect position. That they are more largely and constantly used than the upper extremities, we may be convinced by reflecting upon the activities which make up the lives of men and women at large. And the truth is implied by the more or less automatic character of standing and the movements of progression. The arms and hands are generally exercised consciously.

If, then, it be granted that the limbs most prone to sarcoma are on the whole the most active members, there is the correlative fact that the least active members are the least liable to the disease. The sternum, ribs, clavicle, scapula, pelvis, and vertebræ are passive structures in comparison with the bones of the upper and lower limbs; and when we turn to the skull we see that just those parts in active use are disposed to suffer. Sarcoma of the upper and lower jaws, used in mastication and speaking, is very common, but it only very rarely begins in other bones of the face; and the bones liable in the next degree are those exposed to violence—namely, the bones that form the vertex.

Let us next consider the different degrees of liability shown by different parts of individual bones. We have seen that in central sarcoma the common seats are the epiphyses and not the shafts of the long bones; this is true also, with a greater number of exceptions, of periosteal sarcoma. But the predilection is most marked in certain of the epiphyses; it is not

common to all. The lower epiphyses of the femur and radius and ulna, and the upper epiphyses of the tibia, fibula, and humerus, are with astonishing frequency the ones selected. Now why is this? Perhaps there is some peculiarity in these particular epiphyses that may throw light on the circumstance. I think there is. In each instance the end of the bone invaded is the end where growth is most active. A long bone grows in thickness from the deeper layers of the periosteum, and in length from the extremities of the diaphysis. "Increase in length takes place at the extremities of the diaphysis, the epiphyses co-operating to a very small extent. Ossification, which commences in the centre of the diaphysis, extends towards its extremities until these are separated from the corresponding epiphysis by a thin layer of cartilage (cartilage of conjunction). Growth would cease if this cartilaginous layer ossified like the rest of the bone; but as its margins are encroached upon, an interstitial fresh zone of cartilage is produced by proliferation of the pre-existing cartilage, and a similar round of changes goes on without interruption so long as growth continues. *The two ends of the diaphysis take an unequal share in the increase in length, in the tibia and humerus the upper ends, in the femur and bones of the forearm the lower being most active.*"* Otherwise stated: "in the arm bones the elongation is greater at the end furthest from the elbow joint and in the leg bones at the end which is next the knee joint."† That increments to the diaphysal ends mentioned are the chief means by which the long bones are lengthened is sustained by the results of experiment, but there are other facts which yield substantiation. These are the ends where epiphysal ossification takes place first and where union with the shaft takes place last.

Now the disproportionate frequency of sarcoma at these very epiphyses, or diaphysal ends, can hardly be a fortuitous coincidence. It is found that acute osteo-myelitis and necrosis also affect in most cases these epiphyses.‡ How may the matter, then, be explained? In this wise; those ends of long bones where

* Jones: Op. cit.

† Quain: Elements of Anatomy, vol. ii. p. 114.

‡ Cf. Jones: Op. cit., et Eve: St. Barth. Hospital Reports, 1879.

growth is most active are the parts of bones specially required to bear the strains of function. *It is the unequal exposure of these parts to the work and accidents of life that determines their great liability to osteo-sarcoma.* It might be thought that the tumours start oftenest in the upper end of the humerus, tibia, and fibula, and lower ends of the radius, ulna, and femur, because growth is most active and union of diaphysis and epiphysis latest there, but in reality we must look for the causes of the tumours to the causes of these peculiarities, namely, to the conditions of existence which have entailed a larger share of growth, and its consequence late ossification, at the places mentioned. A little thought serves to assure us that the upper end of humerus sustains stresses of various kinds greatly in excess of those borne by the epiphysis at the elbow joint. Not only is there a much wider range of movement at the shoulder joint, but from this point the whole limb is supported, and the shoulder, in those who perform manual labour, is often made to bear heavy burdens. A similar though less marked contrast obtains between the upper and lower ends of the ulna and radius.

In the lower extremity there exists a quite opposite state of things. Unlike the osseous structures at the elbow joint those at the knee joint are the most hard-worked parts of the entire skeleton. For progression, standing, kneeling, or sitting they are more or less in unremitting exercise, and, what is equally important, are greatly exposed to shocks, contusions, and other injuries. Note that the slender and subsidiary bone, the fibula, was the seat of osteo-sarcoma thirteen times in 165 cases, whereas the primary tibia and femur were the seats forty-six and sixty-seven times respectively. We have seen that three-fourths of the osteo-sarcomas met with occur in the neighbourhood of the knee joint. And the remaining facts are not less in harmony. Among the most active parts of the skeleton are the jaws and conformably sarcoma of these bones is exceedingly common. Out of 280 cases of osteo-sarcoma, 114 were of the face, nearly all in the jaws.* Moreover, in a

* Roger Williams : The Influence of Sex in Disease, p. 14.

majority of cases the upper jaw was affected. Now the larger size of the teeth in the upper jaw implies that it takes the larger share in the work of mastication. The upper set of teeth offers fixed points of resistance to the movements of the lower, and, as might almost have been anticipated, the tumours are generally related to the tooth-sockets. Almost always, too, they are connected with the more active molars, and seldom with the incisors. Unerupted teeth, decayed teeth, and stumps of teeth, are often the immediate excitants of the new growths.

It seems a just conclusion from the facts that osteo-sarcoma is etiologically related in nearly all cases to the effects of functional strain and injuries of various kinds. So concluding, we remember further that about twice as many males as females are sufferers, that the disease is disproportionately prevalent among the working classes, that about half the cases are set down to traumatism, and that the most favourable period of life is between fifteen and thirty-five years of age, just that period when the bones are most in danger of damage from injury. Probably certain constitutional states are contributory with the causes we have noticed. The disease has been ascribed to rheumatism, and is found in association with osteitis deformans. A better perception of the influence of each condition will be obtained by an examination of cases, but before presenting these we may roughly note the conditions of benign tumours of bone.

The benign tumours hitherto considered have not supplied many facts as to their causes. To a slight extent the tumours of this class in bone afford an exception. Though in numerous cases we have no knowledge whatever of the special conditions out of which an osteoma or a chondroma has arisen, yet there are indications that these tumours, like sarcomas, are the consequences of adverse influences acting upon the tissues of origin.

If we take the osteomas first it will be remembered that there are two varieties—the compact and spongy exostoses.

The compact form is mostly seen in the supra-orbital and frontal regions of the skull. Generally they are met with before puberty, and occasionally are the results of injury, but their predilection for the situations mentioned cannot at present be explained.

The ivory exostoses termed odontomata, are well known to be caused by inflammation, carious teeth, or misplaced teeth. An odontoma situated on the socket I have known to follow almost immediately upon injury to a tooth from the dental operation of "filling."

The spongy exostosis is frequently multiple and affects the epiphysal extremities of bones. The majority appear before puberty, from which fact we may infer that its cause is some failure in the vitality of the growing parts of bones. Rickets is a decided predisposing condition and injury may be an adjuvant and exciting cause as the following case, recorded by Mr. Abernethy and quoted by Mr. Stanley,* plainly shows.

CASE 121.—"A youth, about 14 years of age, was brought to me whose back was greatly deformed by hillocks of earthy matter, heaped up upon the spinous processes of the vertebræ. There were exostoses on the os brachii of both arms, and the tendinous margins of the axillæ were converted into bone. . . . There was an exostosis on the pelvis, and various others had formed at different times and disappeared. If, in a forcible effort to accomplish any purpose which his manacled situation often obliged him to make, he accidentally struck his head or any projection of bone, a temporary deposition of earthy matter was always the result. He had the tooth-ache, and an exostosis appeared on the lower jaw."

There is one remaining locality well worthy of notice where exostoses occur. This is the last phalanx of the great toe. Accounts of many such cases are dispersed through the literature of surgery. Often these tumours grow from the extremity of the phalanx under the nail and are seen in young people. The special circumstances of this bone appear adequately to explain its liability to exostoses. Like the parts of bones

* Diseases of the Bones, 1849, p. 214.

subject to sarcoma, the last phalanx of the great toe is much exposed to functional strain, more so perhaps than any other bone of the foot. These tumours have frequently been connected with injuries and the pressure of tight boots. (*Stanley.*) Then the extreme distance from the heart will doubtless often be the cause of nutritive deficiency, which, combining with other conditions, will favour histogenic dissolution.

The chondroma is the most important of the remaining benign neoplasms of bone, and this tumour also shows a predilection for the ungual phalanx of the great toe. The commonest seats are the small bones of the hands and feet, then the long bones, and more rarely it grows from other parts. We thus see in active bones a decided liability to benign as well as malignant tumours. Of the bones of the hand the least active—those of the carpus—are the least liable, and the most active—the metacarpal phalanges—are the most liable. “The phalanges are much more frequently attacked than the bones of the metacarpus, and the carpus seems to enjoy complete immunity. The seat of predilection is the metacarpal phalanx.” Again, the relations of the hands and feet to the nutriment-distributing system is almost certainly an important etiological influence.

Cases Illustrative of the Facts Interpreted.

CASE 122.—*Giant-celled sarcoma of the head of the Tibia.*—“M. S., 67 years of age, of full, plethoric habit, came in December, 1871, on account of loss of muscular power, principally of the right side, which was shortly followed by general erysipelas from which he succumbed in six weeks from the commencement of his illness. During the past twenty-five years of his life Mr. S. had repeated attacks of erysipelas, and chronic ulcers were seated on both legs. Ten years previous to his death, whilst stepping off a street car, he slipped and twisted the left knee, the accident being attended with pain, and succeeded, a few days subsequently, by inflammation, as denoted by slight redness, swelling and stiffness. At the expiration of six weeks, a soft tumour, as large as a hen’s egg, was

detected over the anterior and inner aspect of the joint. . . . The new growth increased very gradually and measured thirty-two inches in its greatest circumference at the time of the patient's decease." (*Gross.*)

(The conditions supplied by the report of this case remind us very forcibly of the conditions we have met with so frequently in cancer and sarcoma of other parts. There is first the age of the patient, then the evidence of chronic degenerating local actions (ulcers and erysipelas) in the region of the structures attacked by tumour-disease, and to these influences are added the exhausting effects of violence at that part which throughout life had been required to perform a disproportionate share of the functions of the skeleton. It should be noted that the patient was of "full plethoric habit," a circumstance probably favourable to neoplasia in the presence of the true causes of histogenic dissolution.)

CASE 123.—*Myeloid tumour in the head of the right Tibia, probably from mechanical shock.*—"About eighteen months previously the patient jumped from a height of two yards, when a distinct snap was felt, apparently in the middle of his right knee joint, at the same time he experienced no pain. Three months after this he was running, when his knee gave way under him, he now had a slight pain. Eight months later, he struck his heel against an iron rod, which caused his knee again to give way, while the injury induced a great deal of aching in the limb. . . . There is scarcely any appreciable enlargement of the upper end of the tibia. The movements of the knee were free and almost painless. Under chloroform the tibia was explored and a maroon-coloured mass exposed. It occupied a cavity in the head of the bone, the size of a hen's egg." (*Jones.*)

(This case serves to show how the impetus of various forces sustained by the lower limbs is distributed to the knee joint.)

CASE 124.—*Repeated injuries to the leg followed by sarcoma (?) of the lower end of the Tibia.*—"This disease occurred in a man aged 38. It had been many years in progress, and was the consequence

of repeated injuries to the front of the leg followed by ulceration of the periosteum of the bone.”—*Stanley: Illustrations of the effects of Disease and Injury of the Bones.*)

CASE 125.—*Sarcoma (?) of the Tibia.*—“This disease occurred in a man aged fifty. It had been twenty years in progress, and had originated in injury to the front of the leg, followed by abscesses and ulceration in the soft parts, and after several years by the growth of a fungus excrescence from the periosteum.” (*Ibid.*)

CASE 126.—*Periosteal sarcoma of the upper half of the right femur.*—“About two years ago, the patient fell and sustained severe injury of upper part of thigh and gluteal region (right); an abscess formed soon afterwards behind the great trochanter, subsequently a sinus remained there for nearly a year; he has since been subject to pain in this region. The swelling at the upper part of the thigh was first noticed a year ago. This hip-joint ankylosed for last sixteen years as the result of coxalgia.” (*Middlesex Hospital Reports.*)

(It appears from these cases that where traumatism is severe, it takes a larger share in determining the *seat* of the tumour.)

CASE 127.—*Myeloid disease in the lower end of the femur.*—“James W., æt. 25, seaman. Two years before, while in London, he struck the joint. The blow caused it to swell and gave him much pain, and he did not recover for some weeks. He then went to sea, and for three months performed his duties, although the limb was weak and sometimes painful; after this it became so much worse that he went into the Leghorn Hospital. He again got better and resumed his work, but, his leg having swollen and being very weak, in October, 1853, he went to the hospital in Malta, where he remained some months; he was then sent to England. On admission into Guy’s, a well-defined tumour was observed at the lower part of the left thigh, and appeared to originate in the condyles of the femur, which were much enlarged.” (*Wilks.*)

CASE 128.—*Subperiosteal sarcoma in lower end of femur.*—“James B., æt. 17. Is employed as a labourer in some boiler works,

He has always enjoyed good health. Last Christmas he noticed that after he had been sitting for some time, upon getting up, a sharp pain came in his left knee on extending it. He had no difficulty in locomotion for a month after this, when he noticed that the movements of his knee were less free, and he also found that there was a considerable swelling on the outer side of the thigh, about four inches above the knee-joint. Patient has a rosy complexion, and is well-nourished." (*Jones.*)

(In the second of these cases we must believe that the tumour was induced solely by excesses of the normal actions of the lower limbs.)

CASE 129.—*Sarcomatous growth, in left clavicle, scapula, and upper extremity in a person disabled on the right side.*—"J. H., aged 20, weaver. He was a strong, healthy looking man, but unfortunately, when a child, had experienced some severe accident affecting the right side of the body, and this had left ankylosis of the right elbow-joint nearly in a straight line with the arm, and atrophy of the muscles in those parts from disease. Slight stiffness of right knee-joint from same cause. Thirteen weeks before admission he had sprained his left shoulder in trying to lift some heavy weight, and in doing so, it suddenly swelled so as to prevent him from working any longer on that occasion. Five weeks previous to admission it began to increase very rapidly." (*Jones.*)

(Here is a case illustrating in a very transparent manner the efficiency of overuse as a cause of tumour-disease. The right upper extremity having been disabled from youth, the left was required vicariously to perform an undue amount of work. The report states that the eruption of the disease in the left shoulder took place after lifting a heavy weight.)

CASE 130.—*Subperiosteal sarcoma following fracture.*—"J. T., æt. 36. In August, 1883, patient was thrown from the end of a railroad platform car, his left leg being caught in an iron upright, by which he was held suspended until released by some bystanders. Dr. Robb saw him at once, and found a transverse fracture of the thigh just above the knee-joint At the expiration of one

month, Dr. Robb found no union of bone, and applied a plaster-of-Paris bandage. At the end of a fortnight the plaster was cut down, and still no union of the fracture. At the time of this dressing there was noticed a change in the circulation about the seat of fracture; and this was supposed by the attendants to be a good omen, because it indicated that nature was making an effort to throw out bony callus. Another plaster-of-Paris bandage was applied for a fortnight, and then this dressing was removed. There was now noticed at the seat of the fracture a decided increase in the size of the limb, and there was no attempt at union. The diagnosis of malignant disease which was made by Dr. Robb was confirmed . . . ” (Dennis : *Philadelphia Medical News*, January 14th, 1887.)

(In commenting upon this case, Dr. Dennis says:—“ This same phenomenon I have seen in a number of cases. In one case, a child fell upon the back of the head, and a sarcoma developed over the seat of a fracture of the occipital bone beneath a large hæmatoma ; in another case a sarcoma developed in the line of union of a simple linear fracture of the skull ; in still another case upon a fracture of the femur.” Such examples help indirectly as well as directly to establish the truth of our conception of tumour-disease. It is a thoroughly consistent circumstance for the discontinuous reproduction of neoplasia to be associated with local inability on the part of the tissues to reproduce themselves continuously, that is, to reunite structures that have become dissevered.)

CASE 131.—*Sarcoma of the tibia showing the influence of child-bearing and suckling.*—“ Elizabeth Warner, aged 30, who came from a miserable hovel at Finchley, was admitted into Saint Bartholomew’s Hospital on June 30th, 1831. She had a swelling, nearly as large as her head, occupying the front and sides of the left leg immediately below the knee, on which it had encroached so much as to render the joint motionless The tumour began to appear in December, 1828, after the patient had hurt the knee by a fall. It had gradually enlarged, without causing pain or any inconvenience, except weakness of the limb, which obliged her to use a crutch. During her pregnancy, in 1829, the disease remained stationary and quiet ; but after her confinement in February, 1830,

whilst suckling, which she continued fourteen months, the tumour became much larger and was occasionally very painful. The patient usually enjoyed good health." (*Lawrence: Medico-Chirurgical Transactions*, vol. xvii. p. 35.)

CASE 132.—*Subperiosteal sarcoma of the tibia showing the influence of child-bearing.*—"Mrs. B., æt. 19. Patient has always enjoyed good health. Nine months previous to October, 1885, patient felt a sharp pain in left leg just above the ankle. The pain lasted but a few seconds, and then disappeared. There were occasional shooting pains in the leg until three months later, when severe cramps occurred. The foot became slightly adematous and the swelling involved the leg. Patient at this time was six months pregnant, and the swelling and pain now disappeared until the child was born. Shortly after parturition swelling and pain returned and the tumour grew very rapidly." (*Dennis: Philadelphia Medical News*, January 14th, 1887.)

(The influence of pregnancy in hastening the growth of mammary tumours was illustrated by several interesting cases. In those cases the increase of the tumours was manifestly due to increased activity of the nutritive processes in the organ concerned. This is probably not the relation in the present examples. The rapid advance of the sarcomas was most likely connected with the diminished physiological resistance of the organism consequent upon the systemic depression succeeding childbirth. The reader will meet with like cases by consulting Courrent: "Sarcoma des os," p. 108, 1886; and Langenbeck: "Archives," vol. xx. sup. p. 329.)

CASE 133.—*Encephaloid tumour of the cranium at the seat of an injury.*—"J. J., æt. 51, a woman of anxious countenance and very pale, was sent to me March 2nd, 1854, with a bleeding fungus tumour of the right side of the cranium. She states that about five years since, in stooping, she injured her head with the metal door of an oven. In healing the wound left a lump the size of a nut, which gradually increased with occasional pain until six months since. At the time the tumour was punctured the result being very free bleeding. Subsequently a protrusion took place at

the seat of puncture, which rapidly assumed the character of a large growth." (*Pemberton.*)

(We have before seen how incisions, contusions, and punctures stimulate the increase of new growths probably by starting fresh dissolutions by histogenesis. A case similar to the present one will be found at page 331, vol. xx., sup., Langenbeck's "Archives.")

CASE 134.—*Tumour of the Sternum of thirty years' duration.*—"A woman, aged 52, had been subject for thirty years to a small swelling on the sternum, always hard from the first and never very tender, except when handled. She could not remember having received any injury to the affected part. The growth increased very slowly in size till five years ago, when it became perceptibly larger. Six weeks before admission into the hospital, the patient fell backwards and hurt her back; the tumour escaped injury, but she was certain that it had increased to twice the size it was at the time of the accident. On August 6th, Mr. Holden removed the tumour; it proved to be a partly calcified sarcoma." (*British Medical Journal*, vol. ii., 1878, p. 358.)

(The indolence of this growth may be ascribed to the seat of the disease. From causes undetermined, it arose in a part which many facts and considerations have shown us to be not well suited for neoplastic changes. As with tumours elsewhere the growth receives accession from the degenerative changes of advancing life.)

CASE 135.—*Osteo-sarcoma of the upper part of the right humerus associated with osteitis deformans.*—"Some years ago I saw a gentleman, between fifty and sixty, very active, tall, thin, and muscular, a master of hounds. For many years before his death, he had curvature of the thighs and legs, exactly like that already described, and stooping of the spine. . . . In the last years of his life the upper part of his right humerus became very large, and as he was riding and suddenly raised his arm the bone broke near the shoulder. The evidence of large tumour now became clear, and I amputated the arm at the shoulder joint. The tumour was a well-marked and

very vascular medullary cancer investing and infiltrating the upper part of the humerus." (Sir James Paget, whose case this was, reports and also gives references to others. See *Medico-Chirurgical Transactions, Second Series*, vol. xlii. 1877.)

(Here, in the association of tumour-disease and the degenerative change called osteitis deformans, which prepares the ground for histogenic dissolution, we meet with unexpected evidence in support of our hypothesis.)

CASE 136.—*Round-celled sarcoma of the upper jaw following injury.*—"The patient, aged 24, was sent to me in January, 1868, by Mr. Harding, to whom he had applied for the extraction of some teeth, thinking to obtain relief thereby. Four and a half years before he had got a blow on the face from a cocoa-nut which broke the left canine tooth, and a year before I saw him, the left side of the face swelled up, but subsided again. . . . When I saw him, there was a soft tumour of the left upper jaw, and a smaller one on the right side, which had appeared about four weeks before." (*Heath: Diseases of the Jaws*, p. 306.)

(Just as the functional activity of the shoulder and knee joints prepares the ground for, or may be the sole cause of, tumours in these regions, so must we think that functional activity was the predisposing cause and traumatism the determining cause of the tumour in the present case.)

CASE 137.—"*Medullary sarcoma of lower jaw in a child. Two successful operations—Return of the Disease—Death.*—Miss M. R., aged 5, was sent to me on September 9th, 1867, with a tumour of the lower jaw. She was the tenth of a family of eleven healthy children, and her parents are strong and robust. She was fat and well-nourished, though thinner than she had been, and in good health until the last week in July (seven weeks before) when her mother noticed that the second temporary molar tooth in the right side was raised above the others, and the gums looked swollen. Her mother took out the tooth, which was quite loose: but the

swelling increased, and the first permanent molar became loose and was extracted." (*Heath.*)

(This is cited as an example of cases presenting difficulties to interpretation by the means we have employed. The essential cause is undeterminable. The embryonic character of the growth, which explains the fatal recurrence, was, I think, related to the tender age of the patient.)

§ 36 *Recapitulation and Conclusion.*

A special interest and value inheres to the contents of the present chapter from the quite unusual clearness with which the process of tumour-disease is demonstrated in the skin. In epithelioma the structural changes incidental to the genesis of a tumour and the conditions of these changes are open to direct observation. Scarcely anywhere else in the body are the opportunities for investigation so favourable. And here, it happens, that where errors of observation are the least likely to occur the facts for our hypothesis are the most convincing of all. The long-standing ulcerations and the oft-repeated injuries which are so commonly precursory to skin-cancer are pre-eminently competent to gradually use up the contained energies of the structural units. The origin, too, of epithelioma in scars, congenital warts, and moles, though a fact of an entirely different order, is seen to be precisely the same in inner meaning. The inferior viability of the tissue of repair, warts, and moles, as compared with original and perfect tissues cannot be doubted, and no consideration so thoroughly agrees with this belief as that every tumour derived from scars, congenital moles and warts, and other tumours, is of low organization. Scars give origin to epithelioma, not to papilloma or adenoma; moles give origin to sarcoma, not to fibroma, osteoma, or enchondroma; warts give origin to epithelioma, not to papilloma; and tumours like adenoma, fibroma, and myoma, give origin not to tumours of full development but to their

embryonic congeners, the cancers and sarcomas. This is a weighty consideration, and every explanation of tumour-disease must recognize and deal with the underlying fact.

Though the conclusions connected with the conditions of osseous tumours were reached more circuitously, these conclusions are not less congruous with the general theory. They are also congruous with the conclusions that have been reached as to the conditions of tumours in the several regions previously dealt with.

From this point our examination might extend to other regions ; we might go on to inquire into the factors of vesical tumours, of tumours of the larynx and of some of the viscera, but I think we have gone sufficiently far afield in this direction. Other classes of phenomena have yet to be disposed of, and their importance entitles them to a proportionate share of our attention.

CHAPTER VII.

THE SECONDARY PHENOMENA OF TUMOURS.

Innocence and Malignancy : Interpretation—The Characters and Distribution of Metastatic Growths : Interpretation.

§ 37. *Innocence and Malignancy : Interpretation.*

When tumours grow as confined and isolable masses and do not recur after removal the clinical term “innocent” is applied to them. If they are not confined but grow by the diffusion of their elements among the surrounding tissues and reproduce themselves there and in distant organs, and reappear after removal, they are said to be “malignant.” One of the first things to notice in this aspect of tumours is the fact that they exhibit many degrees of malignancy. A tumour may be a distinctly separable entity, either bounded by a capsule or seated on a free surface, and yet recurrent if excised. Examples of tumours having these qualities are the essentially innocent but recurrent mucous polypi, and lipomas, and the semi-malignant recurrent fibromas. The latter, although continuing compact in mode of growth, will sometimes destroy the patient by their inveterate return *in situ*. Mr. Bryant* records a case of adeno-sarcoma of the breast in which he operated seventeen times in the course of three years, and yet the disease remained local.

Higher degrees of malignancy are seen in the slow-growing atrophic cancers of the breast where, notwithstanding the un-circumscribed character of the growth and extensive destruction of glandular tissue, the disease for a long time is strictly confined to the substance of the breast. A somewhat limited

* Diseases of the Breast, p. 335.

tendency to spread or to recur is seen in some epitheliomas as those of the lip and scrotum.

Next above these are the cancers and sarcomas which speedily return after removal, multiply in the nearest structures, and before long overwhelm the patient by a reproduction of tumour-elements in internal organs. The highest degree of malignancy is exemplified by rapidly-growing cancers and sarcomas which almost from the first are disposed to spread and infect the body generally. In a case of encephalo-colloid cancer as many as five hundred disseminated tumours were discovered, ranging in size from a hemp seed to that of a man's head.*

Corresponding to these different properties of tumours—the property of growing as a mass distinctly separate from the tissues of origin, the property of spreading locally and then generally—are the effects produced upon the functions and life of the organism. A tumour curable by excision is practically local in its effects and often causes little beyond mechanical inconvenience. Almost the same may be said of the truly malignant growths whose elements are as yet circumscribed. As soon, however, as a tumour begins to greatly enlarge its boundaries and ulcerate, and to disperse its units and infect parts near and afar, the effects upon the organism are congruous. There are now signs of systemic disorder, of the general ill-health which the physician names “cancerous cachexia;” important functions begin to fail, and in this state the patient generally dies.

Sections 11, 12, and 13, have prepared the way for a general interpretation of innocence and malignancy. We start out with the induction that innocence goes with mature development and malignancy with immature development in the cell-elements of tumours, allowance being made for exceedingly rare exceptions. Developed lipomas, myomas, osteomas, neuromas, adenomas, are without hesitation placed in the

* Leidy : *Medical and Surgical Reporter*. Phil. 1870, ii. p. 22.

order of growths that do not recur or infiltrate the tissues, and undeveloped sarcomas and cancers in the order of those that do. Next we remember the *reasons* that have been put forward for the differences of developmental rank shown by the cells of tumours. The cancers and sarcomas, derived respectively from epithelial and connective tissue, are ascribed to a deeper degree of that devitalization of the tissues upon which their dissolution by histogenesis depends. Contrariwise, the loss of vitality in the tissues which leads to the production of a benign tumour is less complete. We found a pretty thorough confirmation of this in the etiology of tumours; the multitudinous conditions causing new growths are seen in excess in the case of cancers and sarcomas, and for the most part are perceived with difficulty or not at all in the case of fully-developed tumours. These considerations will, I think, afford a rational explanation of innocence and malignancy.

The high organization of innocent tumours and the correlates of high organization, are the real grounds of their innocence. The integrated (compact) arrangement of the cells, by not permitting cell-emigration, renders recurrence and systemic infection almost impossible, and these events are further prevented by the capsulation of benign growths. But from the fact of capsulation, from the superior organization of innocent tumours, and from their general etiology, we infer a vital power in the tissues surrounding the tumour such that the growth is not permitted to incorporate itself and spread by infiltration. Observe how conditions the very opposite of these obtain with malignant growths. Their organization is almost invariably inferior and concomitantly the unions between the constituent cells are so weak that emigration readily occurs, and this is assisted by the absence of capsulation in cancers and in many sarcomas. But from the absence of capsules, from the low organization of malignant tumours, and from their general etiology, we infer a weakness in the tissues surrounding the tumour such that the growth is permitted to incorporate itself and spread by infiltration. So

that, in short, the most general cause of innocence is high organization of the tumour-units and relatively high vitality of the surrounding parts, the former condition being determined by the latter; conversely, the most general cause of malignancy is low organization of the tumour-units and relatively low vitality of the surrounding parts, the two conditions being again correlative.

The facts showing degrees of malignancy will be found to come under the rule of these general considerations. When mucous polypi or lipomas return after removal, portions of the tumour capable of renewed growth have probably been left behind. Mr. Curling has reported a case* where lipoma of the spermatic cord returned after repeated operations. In this case the result of an examination of the tumour, removed shortly before the patient died, went to show that the later developments were most likely owing to an admixture of sarcomatous elements. The exceptional metastasis of other benign tumours, as the myxomata and enchondromata, may be set down to the rudimental characters of portions of the tumour mass.

The occasional recurrence of both benign and malignant tumours may also be caused by a recurrence of the original causes.

The tumours known as recurrent fibroids, the cells of which are often oat-shaped, may be taken to represent an inferior but not the lowest stage of organization, and to this inferiority of development their persistent return is almost certainly due. It is very constantly the case that malignancy increases *pari passu* with the increasing simplicity of the cells of tumours. Writing of the sarcomata Dr. Hamilton says :†—"The round-celled types are very malignant, and are apt to form secondary tumours, while the spindle-celled varieties are characterized by a malignancy which is chiefly local." This fact is also attested in the cancers. From the adenomatous type of mammary or rectal cancer to the most embryonic

* Diseases of the Testis.

† A Text-book of Pathology.

encephaloids of these regions there is a fairly regular ascension of power to recur and infiltrate.

It is found, too, and the fact is of much force, that when growths recur repeatedly each return is marked by a reduction of developmental rank in the tumour-cells; and even more interesting in view of these interpretations, the intervals between the recurrences diminish step by step. Sir James Paget says of recurrent tumours:—"The similarity in structure to embryonic texture becomes more strongly marked after each removal and recurrence. . . . A tumour which, at first, might be not unlike the normal fibrous or glandular texture in which it grew, after repeated removal and recurrence becomes softer and more succulent, and in its later growths may seem to the naked eye little more than like masses of yellow or ruddy soft gelatine with blood-vessels. . . . The latter also are usually much more rapid in their progress than the earlier growths; they are generally less well defined, penetrating further and more vaguely among the interstices of adjacent parts and more quickly protruding through the skin or scars over them."* And these are the experiences of others, as of Mr. Eve and Mr. Bryant.† Such characteristics reveal in a recondite way the truthfulness of our conception of tumour-disease. We have said that recurrence, infiltration, and metastasis, are connected with the imperfect organization of tumours and very low tissue resistance. Surgeons and many pathologists explain recurrence by assuming that cells escape removal, and constitute centres of re-growth. There can be no doubt that the whole of the neoplastic elements of diffuse cancers and sarcomas are not as easily removed as those of compact benign growths, and a recurrence from remnant cells must often take place; but this is not, I believe, the true explanation of the majority of cases of recurrence *in situ*. It has been shown that embryonic tumours, as compared with the mature, indicate a *deep* reduction of local vitality and often one of considerable extension among the tissues of an organ

* Surgical Pathology.

† See Diseases of the Breast, p. 338.

or part. This, rather, must be looked to as the main cause of recurrences. *Each operation upon a recurrent fibroid, cancer, or sarcoma, itself brings the local life to a still lower plane, and the recurrences are new processes of reproduction by histogenic dissolution, each reproduction showing the increased loss of vitality by the characters of the products (the tumours), and by the greater and greater readiness of the tissues to dissolve (shorter intervals).* By this view some puzzling facts are at once made clear, such as the occasional sprouting of cancerous nodules at the points of insertion of the sutures after operations upon the breast for carcinoma; and the oftentimes speedy recurrence of the growth *at the seat of the operation-wound* notwithstanding the most sweeping incisions. On this interesting point Mr. Barwell has remarked* that “Occasionally, after operations in which every part of a tumour seems to have been removed, a fresh development sometimes, in the as yet unhealed wound, will grow so rapidly, as in a few days to overwhelm and involve all the neighbouring tissues.” And Dr. Fagge, evidently not satisfied with the explanation in vogue (that recurrences are owing to failure to remove the whole tumour), remarks as follows: “I ought in candour to add that I have not heard that surgeons who adopt the new theory are generally able to obviate the return of the disease by increasing, to whatever extent, the size of the mass which they excise.” To this matter we shall revert in considering the prevention and treatment of tumours.

Though the coherence or incoherence of the aggregate determines in general the clinical behaviour of a tumour, the size and shapes of the cells are circumstances of great importance. The cells of embryonic tumours exist in feeble union with one another, but they are as well of simple form and exceedingly small. Consequently they readily gain access to lymph spaces, vessels, and the interstices of tissue. Reference has already been made (p. 29) to a case of sarcoma in which the secondary tumour-cells had the appearance of micro-organisms, so simple and so minute

* *British Medical Journal*, 1882, vol. i. p. 187.

were they. It is needful to remember as other factors of malignancy that the reproductive power of tumour-cells increases as organization decreases, and that a state of high general nutrition favours the growth of tumours and may make the malignancy acute. And special cases of malignancy must be referred to special circumstances, such as the anatomical and physiological relations of the part primarily implicated, the mixed characters of tumours, &c.

Malignancy in its physiological aspects finds interpretation in our knowledge of the genetic relations of tumours to the organism; in the distribution of metastatic tumours; and in the secretions of certain tumour-cells. By the analogy of their structural developments, it may be concluded that tumours develop physiologically. Indeed, there is positive evidence of this in the milk that has been found in mammary adenomas (p. 32). Cancer-cells of glandular origin may then be supposed to produce degraded secretions corresponding to their degraded structure. This idea was recently advanced by Dr. Heneage Gibbs. It is more than probable that the deterioration of the blood seen in cancerous cachexia is partly due to the poisonous exudates of cancer-cells.

Throughout this attempt to give a rational account of innocence and malignancy, little direct reference has been made to our hypothesis. Every step of the explanations rests, however, upon its propositions, and helps to confirm the truth of them.

§ 38. *The Characters and Distribution of Metastatic growths: Interpretation.*

In the foregoing exposition of innocence and malignancy, an assumption has been tacitly made that now requires to be substantiated. Where a tumour is associated with the appearance of secondary tumours, either near to or remote from the primary, it has been taken for granted that the secondary growths are the descendants of the primary. But the facts which form the basis of this assumption have yet to be set forth.

Of these facts the most cogent are those relating to the structural characters of metastatic or secondary tumours. Whether a secondary tumour is in the immediate proximity of the primary, whether it is situated in the nearest lymphatic glands, or whether it is lodged in the most distant parts of the body, its cell-elements exhibit morphological characters that are clearly indicative of the origin assumed. "The one generalization that stands out conspicuously from the examination of the whole collection of cases is that the secondary tumours (of lymphatic glands and other organs) correspond in structure to the primary, even to the most minute particulars." The metastatic growths of cancer and sarcoma are not only cancerous and sarcomatous but the *variety* of the parent tumour is reproduced. Thus, in the case of an old woman with rectal cancer, there were discovered in the brain three tumours made up of columnar epithelium of the kind composing the glands of the rectum and composing the primary tumour which originated from these glands.* A case also is reported by Dr. Coats, where an adenoma of the thyroid gland gave rise to secondary adenomas in the bones of the skull.

The characters due to degeneration are also repeated in secondary tumours. If the primary growth be a colloid cancer, the metastatic growths will probably be colloid. And the horny degeneration seen in cancers of epidermic origin, or the tendency to fatty embolism seen in mammary cancer, may be seen in the secondary growths. (*Payne.*)

In one or two features of much interest, secondary growths tend to differ from their primaries. Very often it is found that the metastatic products of cancer or sarcoma are inferior to the original in point of structural development. Though the original be a firm cancer or sarcoma, its secondary growths will frequently be encephaloid—an extremely rudimentary form. To understand this we must recall how a highly-organized benign tumour may become the seat of a lowly-organized malignant growth, how the weak tissue of repair may become the seat of cancer, and how in tumours fre-

* Fagge : Principles and Practice of Medicine.

quently recurring the organization becomes less and less with each recurrence. We have also seen that as age advances the tendency of the tissues is to produce embryonic and not mature growths. The inferior organization of metastatic growths is a phenomenon of exactly the same nature, and is attributable to the gradual consumption of the energies of the parent tissue.

In another way secondary tumours are unlike their primaries. They generally differ in their relations to the surrounding tissues. The primary masses of the chief generalizing neoplasms, cancers and sarcomas, interpenetrate contiguous parts and may set up fresh processes of histogenic dissolution in the cells of the structure infiltrated (§ 13). Now secondary are less infiltrating than primary tumours, and apparently do not start fresh dissolutions by histogenesis. "They are usually characterized by a sharply circumscribed border. The tumour grows as a parasite in the part upon which it is engrafted. It stretches and pushes aside the neighbouring tissues, but does not tend to infiltrate them in the same manner as the primary tumour does, and hence has a sharper border."* And it was noted in a case of cancer of the liver, secondary to cancer of the breast, that "there was no division of nuclei amongst the liver-cells, and no appearances indicative of any other change than that of disintegration."† If these observations should be confirmed, the facts may be explained by the views already presented. The intrinsic cause of neoplasia is in the local life, in the life of the part primarily affected, and with the malignant neoplasms it is the feebleness of the part that makes alike possible, the tumour, its infiltrating tendencies, and a spreading dissolution by histogenesis (§ 13). But the offshoots, lodged in some distant organ, are surrounded by tissues whose vitality may be normal, and the physiological resistance therefore greater; hence the characters recorded of secondary neoplasms in the observations just cited.

Thus it is demonstrated that metastasis is owing to the

* Hamilton : A Text-book of Pathology, vol. i. p. 401.

† Thin : Trans. Pathological Society, v. 31, p. 293.

emigration of the *cells* and not the secretions of tumours, and it coincides with this conclusion that metastatic growths are never met with in cartilages or in the cornea, which are impermeable to cells but permeable to fluids. By what channels, then, do these cells gain entrance into new territories? Through the interstices of tissue, by the lymph-spaces, by lymphatic vessels, by blood-vessels, and by open passages of communication between one part and another. If the surroundings of an infiltrating growth be examined microscopically, it can be seen how the tissue is being penetrated by the migratory particles of the primary mass, and it is not rare to see the lymphatic- and blood-vessels choked with cancer-cells. Mr. Arnott speaks of two cases "in which the lymphatics were visibly distended with what seemed to be cancerous material." And in mammary cancer the lymphatics of the skin of the breast may appear as "swollen white cords radiating from the nipple."*

Evidence of metastasis through open passages of communication is furnished by cases of laryngeal cancer. Here cancer-cells may be inspired and take root in the trachea or lungs. In a case of Dr. Moxon, cells inspired from an epithelioma of the trachea lodged at the extremities of the smallest air-tubes and set up multiple secondary growths there.† The same thing may be observed in cancer of the kidney, where the disease spreads down the ureter to the bladder. In a case reported by Dr. Dickinson, a cystic tumour of the lumbar glands burst and scattered some of its particles about the abdomen; these particles became adherent to the peritoneal surface of the viscera and were found *post-mortem* as discrete growths. "They could be readily detached, many of them by the slightest touch. These appeared to be not outgrowths from the serous membrane, but superficial fixtures which had attached themselves after the manner of parasites." Numerous small secondary growths, apparently separated from the primary, are sometimes seen in cancer of the œsophagus; and specimens of cancer of the

* Bryant: Diseases of the Breast, p. 187.

† Trans. Pathological Society, vol. xx. p. 28.

stomach may show "patches of cancer scattered here and there along the small intestines and colon." (*Cripps.*)

These, then, being the means of conveyance of cells detached from the primary, we have next to note the facts as to their distribution. In what localities are the secondary particles mostly deposited? The following groups of observations supply the answer to this question.

Post-mortem examination in 89 cases of mammary cancer* showed that:—

The axillary glands were affected with secondary growths in	91 %
Other lymphatic glands	28.1 „
Liver	39.3 „
Pleuræ	23.6 „
Lungs	15.6 „
Pericardium	2.2 „
Peritoneum	3.4 „
Stomach	1.1 „
Pancreas	1.1 „
Spleen	2.2 „
Kidneys	2.2 „
Supra-renal capsules	1.1 „
Ovaries	5.5 „
Uterus	1.1 „
Bones	5.5 „

In 44 cases of mammary cancer† in which necropsies were made—

The soft parts of the chest were infiltrated in	66 %
The disease had perforated the chest-wall and invaded the thoracic viscera by direct extension in	27.2 „
The axillary glands on the affected side were infiltrated in	90.9 „

* Coupland : Transactions of the Path. Soc. v. 27, p. 264.

† Roger Williams : Middlesex Hospital Reports, 1885, p. 135.

The glands in both axillæ were infiltrated in 22·7 %
 (In 7 of these cases both breasts were
 invaded by the disease.)

The glands at the lower part of the neck (supra-
 or infra-clavicular) on the affected side
 were infiltrated in 25 „

Secondary deposits were found in the Liver				in 20 cases.
„	„	„	„ Lungs	„ 8 „
„	„	„	„ Pleuræ	„ 6 „
„	„	„	„ Femur	„ 4 „
„	„	„	„ Humerus	„ 2 „
„	„	„	„ Retro-peritoneal glands in	3 „
„	„	„	„ Bronchial glands in 2 cases.	
„	„	„	„ Kidneys	„ „
„	„	„	„ Supra-renals	„ „
„	„	„	„ Pancreas	„ „
„	„	„	„ Mesenteric and omen- tal glands in	1 case.
„	„	„	„ Gastro-hepatic in 1	„
„	„	„	„ Peritoneum	„ 1 „
„	„	„	„ Uterus	„ 1 „
„	„	„	„ Ovary	„ 1 „
„	„	„	„ Tibia	„ 1 „
„	„	„	„ Ribs	„ 1 „
„	„	„	„ Spleen	„ 1 „
„	„	„	„ Duodenum	„ 1 „

The distribution of secondary growths was as follows in 83 cases of cancer of the uterus* :—

The Vagina was infiltrated in 72 cases.

The Bladder was infiltrated in 60 cases, and in 31 it was perforated as well.

* Middlesex Hospital Reports, 1885, p. 87.

The Rectum was infiltrated in 21 cases, and in 11 it was perforated as well.

The Pelvic Peritoneum was invaded by direct extension
in 15 cases.

„ Ovaries „ „ „ 14 „

„ Pelvic Connective tissue „ „ „ 5 „

The Sigmoid flexure of the Colon was invaded by direct extension in 1 case.

The Innominate bone in 1 case.

The Ureter in 1 case.

The Adjacent lymphatic glands were infiltrated in 71 %.

There were secondary deposits in the Lungs in 7 cases.

„	„	„	„	Liver	„	7	„
„	„	„	„	Peritoneum	„	5	„
„	„	„	„	Pleuræ	„	2	„
„	„	„	„	Skin of Chest and Abdomen in 1 case.			
„	„	„	„	Heart	„	1	„
„	„	„	„	Kidney	„	1	„
„	„	„	„	Ureter	„	1	„
„	„	„	„	Bronchial glands	„	1	„
„	„	„	„	Tibia	„	1	„

These agree in the main with other observations upon cancer of the uterus.

Thus in 93 cases the Vagina was infiltrated 75 times.

„ 218 „ Bladder „ 83 „

„ 282 „ Rectum „ 53 „

„ 283 „ Ovaries „ 49 „

„ 93 „ Lumbar Glands „ 24 „

„ 93 „ Retro-peritoneal Glands „ 15 „

„ 264 „ Peritoneum „ 18 „

In 283 cases there were secondary deposits in the Liver and Lungs each 22 times.

In 166 cases there were secondary deposits in the Bones and Pleura each 6 times.

In 166 cases there were secondary deposits in the Inguinal Glands and Stomach each 5 times.

In the Bronchial glands and Kidneys 5 times.

„ Thyroid-gland, Mediastinal glands, and Heart, 3 times.

„ Brain, Supra-renal capsule, Glands of mesentery, Jejunum, Lumbar vertebræ, and Skin, each twice.

„ Gall-bladder, Dura mater, External genitals, Muscular system and Mamma, each once.*

Let us now examine severally the facts these figures bring to view, and while reinforcing them with additional facts, attempt a rational interpretation.

It is clearly brought out by the foregoing tables that the most frequent seats of metastasis in cancer are the tissues of the organ first involved, the neighbouring parts, and the nearest lymphatic glands. The mamma or the cervix uteri may be entirely transformed into neoplastic matter; the soft parts of the chest in mammary cancer, and the vagina, rectum, and bladder, in uterine cancer, are invaded by direct extension. These facts our hypothesis will explain. The disease being local in origin, and being the outcome of local weakness, the tissues of origin offer the most favourable soil, by reason of their feebleness, for the propagation of the tumour-cells. But the parts adjacent to the tissue of origin are not outside the sphere of those local influences which have occasioned the disease; hence the parts adjacent also offer a favourable soil should their texture and vascularity be suitable. In 66 % of cases, the soft parts of the chest were implicated in mammary cancer. In 83 cases of uterine cancer, the vagina was implicated 72 times, the bladder 60 times, and the rectum 21 times.

Accounting, as we do, for the remote extension of cancer or sarcoma by the supposition that tumour-cells are carried away with the outgoing lymph and blood, it concurs with what has gone before that the *nearest* lymphatic glands are among the most common of all places for the deposition of secondary tumours. These organs are in immediate functional associa-

* Billroth und Leucke : Handbuch der Frauenkrankheiten.

tion with the structures that give birth to the primary tumour ; in them the migrant germs conveyed with the lymph are first arrested, and in them the nutritive material for increase is abundant. It has been seen that low nutrition is a cause of the genesis of tumours, and that high nutrition aids their growth.

Less frequently, the more distant lymphatic glands become involved ; but holding the next place among the parts liable to metastatic deposits are the liver and lungs. One of the tables above shows that the liver was affected with secondary tumours in 39·3 % of 89 cases of mammary cancer. But whatever the situation of the primary growth, the liver and lungs are far above other viscera in the frequency with which they are selected ; and this whether the primary growth be carcinoma or sarcoma. Then come the pleuræ, heart, spleen, kidneys, bones, brain, etc. “Sarcoma is especially prone to affect the lungs and pleuræ, and it also attacks the heart, liver, kidneys, spleen, distant and disconnected lymphatic glands, brain, bones, muscles, and subcutaneous tissue” (*Butlin*). Now the reason for these general facts respecting the distribution of secondary tumours is not far to seek if we base our reason on the contents of the preceding pages. The accessible channels of communication with the organic systems, offered to the segregated particles of a primary tumour, are the venous blood- and lymph-vessels. Arteries, owing probably to their texture, stubbornly resist the encroachments of malignant tumours, and only at a late stage in the history of a case of malignant disease will there be found any signs of yielding. The venous and lymph-streams, however, are open, directly through small veins, through capillaries, and through lymph-spaces ; and since these streams are everywhere in the body directed to the lungs towards the lungs the secondary particles will be carried. Should the primary tumour be in direct relation with the abdominal or portal venous system, then the particles on their way to the lungs must enter the substance of the liver. Here, or in the lungs, or in both organs, their progress will be stopped. The capillaries of these viscera are the first capillaries encountered, and the tumour-cells meeting here with a

plentiful supply of nutriment, their growth and propagation will be favoured.

Turning now to the other localities, we find them to be the heart, spleen, kidneys, brain, and bones, but these are implicated with nothing like the frequency of the lungs and liver. Can this relative infrequency be explained? To reach the spleen, or kidneys, or brain, by way of the vascular system (not by direct extension), the cells of a tumour must pass, as we have seen, through the capillary system of the liver or lungs, or through the capillary systems of both these organs. But here they are usually arrested and grow with fatal effect. The liver, lungs, and pleuræ are often studded throughout with metastatic growths. Yet when, as occasionally happens, the germs reach the left side of the heart, their dissemination by the systemic arteries becomes possible, and they are found deposited in the spleen, brain, or kidneys. In accounting for the comparative immunity of the heart, we must bear in mind that the secondary particles are not admitted into its substance until they have obtained access to the arterial system. They may, however, be sown in stagnating blood within the heart-chambers. Cancer has been seen growing in clots lodged in the right ventricle (*Moëon*), and in the right auricular appendix and left ventricle (*Payne*).

How do the cells of tumours, as of cancer, reach the substance of bone? This is a somewhat frequent situation of secondary growths, especially in scirrhus of the breast. The extension to bone may be direct, or indirect by way of the systemic blood-vessels. It is not usually until a late stage of the disease that visible signs of metastasis to this tissue are present, but it has been pointed out by Dr. Snow* that tenderness and thickening of the humerus on the same side as the breast diseased may be discovered earlier. It is "found in the majority of cases of ordinary breast scirrhus comparatively early in the course of the disease, and simultaneously with commencing enlargement

* *Lancet*, 1880, v. 1, p. 12.

of the axillary glands." The marrow of bone, from its softness and succulence, is doubtless a very suitable breeding-ground.

That the general distribution of secondary tumours is determined by the broad anatomical and physiological conditions considered, appears to be an unassailable conclusion. But the differences of distribution in different cases and groups of cases will depend on minor anatomical and physiological conditions. Thus, the frequency with which the pleuræ and lungs are involved in mammary cancer is owing to the position of the mamma on the chest-wall. Again, in cancer of the stomach, the liver is involved in "a proportion twice as great as that of such deposit in the lymphatic glands adjoining the stomach, and thrice as great as that of secondary cancer of the lungs;"* and here the explanation lies in the relations of the stomach and liver. There are many exceptions to the rule that lymphatic glands are the organs most commonly affected by secondary tumours. "A round-celled sarcoma of the tonsil will certainly affect the lymphatic glands, but a central round-celled sarcoma of the tibia will not affect them" (*Holmes*). "Sarcomas of the eye, the upper jaw, the bones, the larynx, and the breast, rarely or never affect the glands. But those of the foot, tonsil, the testis, and, probably, the kidney, affect the glands certainly and in most instances early" (*Butlin*). "All tumours of the tonsil, whether sarcomas or carcinomas, affect the glands, and all tumours of the testicle alike attack the glands." To understand the distribution of secondary tumours in any individual case, it will obviously be needful to consider the characters of the primary growth, its seat, and its relations to near and remote organs.

Surveying comprehensively the facts we have just dealt with, it is perceived that the common seats of primary malignant disease are scarcely ever the seats of secondary malignant disease, and that the organs most liable to the secondary

* Brinton: Diseases of the Stomach, p. 245.

affection are least liable to the primary affection. This is a generalization eminently in harmony with the doctrines our data have obliged us to embrace. It thoroughly coheres with the induction that tumours are the consequences of locally incident and environmental actions ; and it is in exact concurrence with the conclusion that innutrition favours the genesis of tumours and high nutrition favours their growth. Without depreciating in any degree the influence of the causes we have recognized of the distribution of secondary growths, there is, I think, no doubt that the central positions of the lungs, liver, spleen, kidneys, &c., confer upon these organs a special suitability as nutritive media for the growth of tumour-cells. Secondary tumours of the breast, testicle, or tongue, are not known ; and it has been doubted if they ever occur in the stomach or uterus. And besides the almost exclusive distribution of secondary tumours among the highly nourished central viscera, we find that in metastasis to osseous tissue the bones near to the trunk are the chosen seats. “ Out of 650 necropsies of cancer of the breast which give full details as to the distribution of the secondary growths, there is not a single case where the hands or the feet were affected, not one of disease of the radius, ulna, or fibula, and only one of the tibia. In contrast with this, the femur was affected either by spontaneous fracture or distinct deposit of cancer 18 times, the humerus 10 times.”* It has been observed of primary sarcomas that when situated near to the trunk, they are, with few exceptions, more malignant than when situated in distant bones (*Butlin*).

Cases Illustrative of the Facts Interpreted.

CASE 138.—*Carcinoma of the cranial bones, of the dura mater, of the clavicle, ribs, humerus, bronchial glands, liver, and pleura, following cancer of the breast.* Inspection made thirteen hours after death.—“ On the left side of the frontal bone, near the vertex, was an irregular projection, about a quarter of an inch in height, and two inches and a-half in diameter, yielding beneath the finger. The scalp was adherent at this part. Near the occipital bone was a

* Stephen Paget : *Lancet*, vol. i. 1889.

similar, but rather smaller tumour, on the parietal; and in the various parts of the skull others were observed. The dura mater was slightly adherent, but only at the parts corresponding to the diseased bone. The diploe was more extensively destroyed than the inner or outer plates, and the margin of the carious portion was very irregular and brittle. On the left mamma was an irregular hard cicatrix, extending into the axilla; and the left arm was very œdematous. The whole of the outer portion of the clavicle was destroyed, except the cartilage, and was infiltrated with cancerous deposit. The first, second, and third ribs were involved in a firm mass, and destroyed near the axilla. The growth extended, though slightly, to the pleural surface. The cervical glands were infiltrated. The humerus was fractured in removing the corpse. On tracing the shaft of the bone downwards, the broken part was found to be situated about five inches from the head. The shaft was exceedingly thin, and was surrounded by cancerous growth. This substance filled the medullary cavity, and on section of the bone, was found to extend to the head, destroying nearly half of the cancellated tissue, but covered by smooth and apparently healthy articular cartilage.

“In the pleural cavity were a few ounces of serum, and on the serous membrane several firm and white tubercles. In the liver were several carcinomatous tubers. The uterus, ovaries, and other viscera, were healthy.” (*Habershon: Trans. Path. Soc.*, vol. vi. p. 321.)

CASE 139.—*Subcutaneous Cancer, secondary to Cancer of the Glans Penis.*—“An agricultural labourer, æt. 70 years, had all his life enjoyed robust health. During the three weeks preceding his admission, a number of hard, irregular lumps, mostly about the size of a nut, appeared under the skin on different places. On admission, a number of these tumours could be seen over many parts of the body. They were numerous over all parts of the trunk, particularly on the sides of the thorax and over the axillæ. A good many lay about the umbilicus. These were most numerous wherever absorbent glands existed. Many occupied both groins, and the inside of the thighs at their upper parts. The secondary tumours were encephaloid.” (*Dickinson: Trans. Path. Soc.* vol. xiv. p. 240.)

CASE 140.—*Traumatic Malignancy; Sarcoma of the sole of the*

right foot.— “At the margins of the cicatrix in the foot were several little nodules of recurrent disease ; but the portion of skin brought down to cover the wound was healthy. In the groin, the femoral glands formed a mass of disease of the size of a small orange, and about the upper part of the body were a few small subcutaneous nodules. She was greatly emaciated. During the next few weeks hundreds of small nodules appeared beneath the skin of the trunk, the limbs remaining free. Symptoms of internal complication rapidly supervened, and she died, nine months after the original operation.

“At the *post-mortem* examination the subcutaneous nodules described were found to be little masses of sarcomatous material, lying beneath the skin. The surfaces of both lungs were found studded with nodules as large as peas. These nodules were just beneath the pleuræ, and apparently growing beneath the pericardium and the endocardium. The right femoral and inguinal glands, and the lumbar glands of both sides, were converted into masses of disease. Secondary growths were thickly studded in the kidneys, pancreas, and liver. The intestines presented an extraordinary appearance, looking as if they had been thickly covered with boiled sago, caused by thousands of nodules in the peritoneal coat. The mesenteries were similarly affected, and the great omentum was converted into a white nodular mass, weighing four pounds.” (*Harrison Cripps : British Medical Journal*, 1882, vol. i. p. 653.)

CHAPTER VIII.

THE EVIDENCE FROM THE EFFECTS OF TREATMENT.

§ 39. *The Curability of Fully-developed Tumours.*

If a lipoma, fibroma, or adenoma, be excised, and the whole of the growth removed, we do not look for a return *in situ*. The disease is acknowledged to be curable by this means. But no other certain means of cure is known. We cannot, for instance, dissolve the tumour by the internal administration of chemical agents. To such agents the new growth behaves like the normal tissues, and so it does also to locally-applied agents in the shape of escharotics, the cautery, electricity, &c. These effects of remedial measures are the legitimate consequences of the nature of the disease. It has been here argued that a well-organized tumour is local by origin and cause, and is a definitely-limited and segregated mass; it is therefore entirely consistent that excision is curative. And that well-organized tumours exhibit the same reactions as the natural tissues to external applications, falls in with the conclusion that tumours are reproductions of the tissues.

§ 40. *The Incurability of Embryonic Tumours.*

If an incompletely-organized fibroma, sarcoma, or cancer be excised, we expect that it will return *in situ* or elsewhere. The disease is acknowledged to be incurable by any known means. This has passed into a truism, but it is a truism which calls for some reservations. Epithelioma of the lip, scrotum, and certain other parts, and occasionally some sarcomas, are curable by excision; in proof of which many cases could be adduced. Are these effects of remedial measures in the case of the embryonic tumours consonant with our conclusions as to the nature, origin

and causation of such neoplasms? Completely so. Being like the benign growths, local by origin and cause, it should follow that under special circumstances excision is curative. If the tumour has been caused by definitely-local actions, if it be extirpated at an early stage while infiltration is as yet limited, and if there be no repetition of the causes, a permanent cure of the disease is conceivable. But when the causes are indefinitely-local, when the infiltration is widespread, and when the local feebleness of the tissues is such that fresh dissolutions by histogenesis readily occur from advancing age or new incident actions (as the wounding by operation), then a cure by excision is not a reasonable expectation. And from the nature of cancers and sarcomas—being offspring of the tissues—their resolution by drugs given internally is not to be expected; nor is there good evidence that any attempt ever made to cure the disease in this manner has been availing. Furthermore, the effects of escharotics and the cautery are predeterminable from the views enunciated. Sir William Savory has written as follows:—"The most frightful ravages I have ever witnessed in cancer have followed the application of caustics."*

* *Lancet*, vol. i. 1879, p. 37.

CHAPTER IX.

HEREDITY AND TUMOUR-DISEASE.

The Evidence *a posteriori*.—The Evidence *a priori*: Conclusion.
General and final Conclusion.

§ 41. *The evidence a posteriori.*

Among physicians, but more generally among the non-medical, there is a rooted conviction that cancer is frequently an inherited disease. This belief is so far-reaching and momentous in its effects upon practice, that we ought to inquire very searchingly how far the belief is true.

Sir James Paget probably assigns a larger influence to inheritance in the etiology of cancer than does any other observer. Indeed, he is one of those who, at the time of the memorable "Discussion on Cancer," saw in the very nature of the disease a necessity for hereditary influence. On that occasion Sir James said :—"I am disposed to hold that it is not possible to conceive of the origin of cancer, or, I would add, of any disease of like kind, except by inheritance."* He places the frequency of inheritance at very nearly 25 % of 322 cases.† Mr. Bryant, pursuing the same method of inquiry in 600 cases of mammary cancer, found evidence of inheritance in only 12 % of the whole number. A still lower figure is given by Gross, the histories of whose patients showed hereditary influence in 9·7 %. It is placed by Gusserow at 7·6 %, and by Sibley and Barker at 8·2 % in uterine cancer. A distinct family history of cancer was traced by Mr. Bowerman Jessett in 2·8 % of 860 cases. Positive support to the assumption of hereditary influence in the causation of cancer was obtained by Dr. Fink in 8 out of 87 cases.‡

* Transactions of the Pathological Society, vol. xxv. p. 317.

† Surgical Pathology, p. 786. ‡ Zeitschrift für Heilkunde, Bd. ix. Hft. 6.

These several results have been obtained inductively by those who are believers. Now let us see what conclusions have been reached by those who, seeking truth by the same means, are yet disbelievers.

Mr. Allingham says* :—"I am in accordance with those who do not consider cancer as an hereditary malady; it is true that there are very few families in which cancer has not appeared more or less remotely, but that is only because cancer in some form is so common in human beings. Although I always put the question, it has comparatively rarely happened to me to find that the father or mother, or even grandfather or grandmother, has suffered from the disease. Often uncles or aunts, or brothers or sisters, and still oftener cousins and more distant relations have suffered from cancer; but the question of heredity is not thereby affected."

A like opinion has been arrived at by Dr. Herbert Snow, who supports his opinion with the following observational results† :—"Of 519 patients affected with mammary scirrhus, 94 gave some family history of cancer, 425 denied any such. Of 295 patients with uterine cancer, 37 gave a family history; 258 had none. Of 204 cases of epithelioma in various superficial sites, 31 were placed in the former class, 173 in the latter. Of 57 cases of sarcoma, 7 gave a family history, and 50 denied any hereditary taint. Thus, of 1075 cases of malignant disease in its various forms, there was some account (not by any means of hereditary transmission) of more than one individual in a family having been affected by diseases of a certain class (not even by the same disease) in 169 instances only, or 15·7 %. This, again, is the most liberal estimate possible, for all forms of blood-relationship are included; and 22 of the above are marked very doubtful."

Dr. Winiwarter‡ states that inheritance is excluded in almost all his cases; and Mr. Holmes writes thus concerning the influence of inheritance in cancer of the tongue :—"In my own collection the evidence on this question is as follows—family

* Diseases of the Rectum, p. 285. † *British Medical Journal*, vol. i. 1885.

‡ Beiträge zur Statistik der Carcinome.

taint is distinctly negatived in 20 cases, is simply negatived in 22, is only positive in 1, is doubtful in 4, and no statement on the point is made in the rest. These conclusions are strengthened by the results of an analysis of Mr. Morris's collection of 61 cases." And speaking of cancer of the tongue, Mr. Butlin writes that "only an exceedingly small proportion of patients with carcinoma of the tongue are conscious of the occurrence of carcinoma in other members of their family." Of tumours, generally, the same observer remarks that, "The laws of inheritance of tumours, if such laws be admitted to exist, are singularly limited in their extent, and appear almost eccentric in their incidence."

Before we assay this evidence for whatever of truth it contains, it will be well to look at the question from the *a priori* point of view.

§ 42. *The evidence a priori.*

Is the influence of heredity in the causation of tumours deducible from the conclusions we have formed as to the nature of neoplasia? And is hereditary influence rendered probable from the general etiology of tumours? In my volume on "Dissolution and Evolution and the Science of Medicine," I have submitted the argument that non-congenital or acquired diseases are for the most part not heritable. True or acquired diseases being with few exceptions disorganizations (dissolutions) of the substance of the body, and inseparably related to environmental actions, they cannot exist apart from these actions, and cannot therefore be transmitted. On the other hand, a normal, or newly-acquired and well-organized character, by reason of the fact that it is *incorporated with other functions and structures*, becomes freed from the external agencies which induced it, and attains to independent existence; it, therefore, is transmissible. When formerly arguing to this effect, I had not pursued my inquiries into the nature and origin of neoplasia to their present development, and it was left undeterminable how far tumour-disease might be an exception to the non-transmissibility of acquired diseases in general (Op. cit. p. 230). But the clearer insight now afforded into the meaning and conditions

of neoplasia, assures me that it is not an exception. A tumour is hardly more incorporated with the existing functional and structural arrangements than is a tape-worm living in the intestines. I have already shown (op. cit.) that the process involved in the genesis of tumours conforms to the formula of dissolution, but that it does so is now almost self-evident in the light of more definite conceptions. Both by their morphology and by their clinical characteristics, it is seen that although tumours are descendants of pre-existing tissue, the process of tumour-genesis is a true dissolving away of old functional and structural attachments. There is, it is true, a reorganization and redevelopment of the tumour-substance, but this is distinct from the process which gave birth to the tumour and is independent of and in opposition to development in the organism. Reasoning deductively, therefore, from the nature of neoplasia, we must infer that tumour-disease is not transmitted by inheritance.

What, now, is the inference to be drawn from the general etiology of tumours? Does this encourage belief in the influence of heredity? We have learnt that the causes of benign tumours are often too slight to be detected, but that the cancers give evidence in nearly all cases of the operation of causes whose efficiency is intelligible and certain; and these causes are locally-incident actions. We find that in cancer of the lip and tongue there is always sufficient in the life-conditions of the patient to account for the disease without the assumption of hereditary transmission. And it is seldom that this is not the case with cancer of the breast, uterus, and other parts. It is, consequently, not wanted that we should fall back on the hypothesis of transmission by descent, and the needlessness of the hypothesis must be set against its credit. So that *a priori* considerations are altogether unfavourable.

It now remains to weigh the *a posteriori* evidence. The first criticism to be passed upon the facts of those who share in the belief that tumours are inherited is a very important criticism. Accepting as valid the evidence adduced, this evidence is yet so spare and inconsiderable a quantity that we can hardly allow

it any appreciable weight. The reader will have observed that the differences in the results of the several observers are extreme. Sir James Paget discovers inheritance in 25 % of cases; Dr. Gross in 9·7 %; and Mr. Jessett in 2·8 %. Surely if such figures, when averaged, prove anything, they prove that the influence of heredity is too faint to be of any practical moment.

But can this evidence, so far as it goes, be accepted as valid? I think not. In every instance, apparently, the recurrence of environmental causes in members of the same family has been entirely left out of account, and this omission, seeing the prevalence and aptitude of such causes, must reduce the testimony to a vanishing quantity. In a disease as common as cancer, too, it would be wonderful if we did not meet with some cases among blood-relations. But the results are gravely vitiated in still other ways. Sir James Paget does not assume any relation either of locality or structure in the diseases transmitted. One form of cancer will be transmitted as any other form. "The cancer of the breast in the parent appears as cancer of the lip in the child; the cancer of the cheek in the parent becomes cancer of the bone in the child; there is in these cases absolutely no relation at all of place or texture."* Then, among the relatives of those who suffer from cancer are included such collateral connections as aunts, uncles, and cousins; inheritance is sought for among those from whom the disease plainly cannot be inherited. Without any further allegations and proofs of inadequacy, I think we may decide that the results we are considering are virtually negative, and when the conclusions of Mr. Allingham, Dr. Snow, and others, are remembered, the whole argument *a posteriori* must be judged to disfavour the doctrine of inheritance. But the argument *a priori* is to the same end. We must then ultimately conclude that tumours are not transmitted by descent.

§ 43. *General and final Conclusion.*

It is not pretended that every ascertained fact of tumour-disease has now been noticed, nor that every ascertained fact

* Trans. Path. Soc. vol. xxv. p. 318.

comes within the explicative power of the principles unfolded. But it is alleged that the hypothesis we have designed to test and develop is not at variance to any important extent with the established data. It is also alleged that the hypothesis makes neoplasia as intelligible as any fact in biology, and makes possible the elucidation of the great problems connected with tumour-disease. This is sufficient to justify our acceptance of it. We may, I think, believe that it provides a true picture of the phenomena inquired into. Certainly, every rival hypothesis is ruled out of hearing until it is shown to be equally illuminating and comprehensive. If we have committed ourselves to and still advocate the humeral theory, or Cohnheim's theory, or the hypothesis that cancer is a bacterial disease, or is the consequence of diminished resistance of basement membranes, or is caused by local excess of nutrient matter (*Roger Williams*), the task which each of these assumptions must accomplish before it can be accredited is now plain enough. It must not simply be reconcilable with a fact here and there of the morphology of tumours, but with all the facts of this class, and with the whole of the still larger class of clinical facts. That in the case of any one of these means of explanation even a good beginning will be made in this direction seems to me exceedingly improbable.

Since we may attach so high a degree of certitude to the hypothesis we have considered, it is warrantable to attempt to draw some practical deductions.

CHAPTER X.

PRACTICAL DEDUCTIONS.

The Prevention of Tumour-disease.—The Treatment of Tumour-disease.

§ 44. *The Prevention of Tumour-disease.*

That tumours are not of spontaneous origin but acquired, is established by two bodies of evidence—the facts as to causation and the argument from heredity. Cases show us the operation of factors of proved competence, and we have seen that there are no grounds for believing that tumours are or can be inherited. Thus we are prepared to surmise, in opposition to current opinion, that tumour-disease may not be wholly unpreventable.

But if the contents of chapters IV—VI. be recalled in their totality, this surmise immediately strengthens into conviction. It becomes abundantly evident that the most effective of the causes of tumours in general are avoidable and removable. Diseases are prevented by avoiding and removing causes. It is true that certain predisposing causes, such as age, and the relations of tumours to the vascular system, are almost beyond the range of a practical prophylaxis. But setting these, and probably a few others, aside, there yet remain among the avoidable and removable class nearly all those causes that are in themselves efficient.

Since it has been shown that the tumours of each organ or part originate by means that are more or less special for every instance, it follows that in attempting to prescribe the means of prevention the tumours of each part must be considered separately. There are, however, some considerations applicable to one of the general conditions of tumour-disease that it is advisable to advert to before we go further.

Foremost among the general conditions of tumour-disease is the age of the subject. Age is a strong predisponent of both cancer and sarcoma, and we are led to think, from the nature of neoplasia, as well as from the facts of certain cases, that age alone will sometimes be efficient. It rarely happens, however, that some special cause is not superadded. But the important thing to remember in connection with age as a condition of tumour-disease is its relativity. Some men are old at forty while others are young at fifty. Age is decided not only by the years but also by the life that has been lived. The cancerous tongue of a man of thirty-five is older than the healthy tongue of a man of eighty. In thinking of age as a cause of tumour-disease, we must have in mind the number of years in relation to the life-experiences of the organism. And, therefore, in order to diminish the favourableness of advancing years, both the local and general life of the tissues should be carried on without undue waste of those powers through which the individualities of the whole and its units are maintained. *Hence it appears that while age as a predisposing cause of tumour-disease is irremovable, it is yet possible to increase or weaken its force.*

Turn we now to the prevention of tumour-disease as it occurs in special situations. Following the order of chapters IV—VI., cancer of the lips comes first to be entertained. The evidence as to the indispensableness of the recognized causes of labial cancer is so sufficing, that in the absence of local irritation, non-appearance of the disease may be confidently predicted. Nowhere else in the body is the prepotent influence of local irritation over all other conditions as clearly and conclusively shown as in cancer of the lips. Without the use of the pipe, and without other local circumstances competent to exhaust the local contained life-energy of the tissues, the general and predisposing conditions would, we may conclude, be entirely nugatory.

Like vaticinations are necessitated as respects cancer of the tongue. Abstinence from, or the strictly moderate use of, tobacco and alcohol, and the avoidance of every other source of

lingual irritation, would, with the greatest probability, prove completely preventive.

We have seen how intemperance is probably the chief inciting condition of cancer of the pharynx, œsophagus, and stomach. It seems impossible to doubt the preventibility of these diseases, and that future research into their causation will show them to be rigorously dependent on violation—often gross and persistent—of rational dietetics.

Of the prevention of cancer in the lower divisions of the alimentary canal, we must speak for the present with less confidence. But the cases and arguments which have been adduced certainly justify the expectation that the essential causes are to be found in the alimentary environment, and that they are not outside the scope of measures of prevention.

The very nature of the prime causes of tumours of the breast give us pause in approaching the great question of their prevention. How can we ever hope to keep in abeyance the development of a disease whose mainsprings are so deeply laid in the established order of social life? It is only too plainly deducible from the facts that the risks of mammary cancer vary directly as the fecundity, other things being equal. Fortunately, other things are not always equal, and the qualifying circumstances afford a measure of hope for many individuals. But our aim is the intelligent prevention of cancer of the breast. For this the physical organization of woman will require that she bear less heavy burdens in her capacity of mother. The individual woman must not be called upon to take as large a share as at present in continuing and increasing the race, and the conditions of her life must be so adjusted that her office may be discharged without entailing physiological bankruptcy. The first requisite in any measures designed to lessen the terrible frequency of mammary cancer, will be to watch over the expenditure of the physiological capital, in the first place by controlling fecundity, and in the second by diminishing its cost positively and relatively (see p. 138). For the present, we must leave the further inquiry as to how far and in

what way these desiderata may be practically realized ; but it is opportune to point out here how potent an influence may be exercised by the supervision and restraint of the function of lactation.

Following this, the first principle in the prophylaxis of breast-cancer, come the recognition and avoidance of the accessory and determining causes. With the evidence before us of the part which destructive inflammation of the breast plays in the genesis of cancer, the prevention of such inflammation assumes great importance. And here, it will be remembered, how very often the perversions of mammary function associated with depressed nipples are succeeded by cancer ; and how depressed nipples may in turn be traced to the pressure-effects of the corset.

The causes of cancer of the cervix uteri are germane to the causes of breast-cancer ; therefore our preventive procedures will be nearly the same for one disease as for the other. But as the act of coitus, apart from its remote physiological issues, is probably the main factor in the etiology of uterine cancer, prevention in this disease will apparently be a less complicated affair than the prevention of the mammary affection. I mean that it will be possible to employ effectual measures without serious conflict with the appointed purposes of monogamic marriage. The disease may be avoided, and yet the individual man and individual woman need not lose in productiveness.

In the prevention of cancer of the external genitalia, the special causes of the disease in these parts will require attention, and the same precept applies in uterine myoma (see §§ 29 and 30).

With the moderate and not impure use of the male organs of generation, we shall be reluctant to think that cancer here can arise independently of external violence and the irritation of foreign matters. If unrestrained indulgence of the sexual appetite is, as we have been led to conjecture, the

root-cause of malignant disease of the testicles, then wherever there is congenital defect of these glands or other causes of their weakness, a more careful control of the sexual propensities will be called for. Those whose testicles have not descended into the scrotum, or who suffer from other abnormality of these organs, should exercise strict moderation.

In the case of scrotal cancer, the preventability of malignant disease has been demonstrated by results and put beyond need of discussion.

The prophylaxis of epithelioma, or skin-cancer, must mainly consist in the avoidance of external irritants. Agents of this sort are seldom undiscoverable in cases of cutaneous epithelioma. Even where warts, moles, benign tumours, and cicatrices, are among the predisposing conditions, there is yet nearly always present some form of external irritant which actually determines the cancerous or sarcomatous change. In many cases, as we have seen, the irritation is often repeated or is continuous for long periods. It is the indication of a large array of facts that particular care should be taken to protect from hard usage such inherently frail structures as cicatrices, warts, moles, and tumours.

Of all forms of malignant disease, osteo-sarcoma is apparently the least promising from the standpoint of prevention. The intimate dependence of the disease upon exhausted local tissue-life is shown unstintingly; but a considerable proportion of the observed cases have been immediately due to traumatism. Though the causes of the disease are recognizable, it will not always be practicable to avoid them. A proper regard to the wear and tear of those parts of the osseous system most subject to osteo-sarcoma, will insure a decreased liability; and it will do so first by lessening the tendency in over-used structures to discontinuous growth (histogenic dissolution), and next by weakening the influence of traumatic injury as a provocative of histogenic dissolution.

A probably-important *general* condition of tumour-disease now falls to be considered. What inference as a causal agent must be allowed to high systemic nutrition? The very frequent association of cancer of the breast and uterus with obesity and overfeeding, will dispose us to regard the association as not without etiological significance in face of the dependence upon nutrition of all organic growth. Neoplasia is a form of organic growth. Already it has been mentioned (p. 65) that high nutrition *per se* cannot be supposed to occasion histogenic dissolution, but that in the presence of competent causes it will be a favourable circumstance. Whenever, from intercourse with the environment, the potential energies of a part have reached the stage of depletion which favours dissolution by histogenesis, a rich supply of nutrient matter will, presumably, hasten the process. That it hastens the growth of a tumour has been demonstrated, and the probability that it facilitates tumour-genesis warrants the inclusion of this condition among the factors to be considered in preventing tumour-disease.

The contents of this section may be summarized by saying that the prevention of both benign and malignant tumours rests on the application of our knowledge of the environmental causes. These causes, we now know, are most varied in kind, in degree, and in mode of co-operation.

§ 45. *The Treatment of Tumour-disease.*

The subject remaining for consideration is divided by the two great classes of tumours, the benign and malignant. Benign tumours are for the most part readily curable, and therefore there is little to be said concerning the treatment of them, where treatment is required. Their curability by excision is what might be expected from our conception of their nature, and though excision is not ideally adequate, there is difficulty in devising a more suitable means of riddance for a redundant, isolable, mass of tissue whose cause has acted once for all. But

ablation by the knife falls short of perfection in that the injury done by the operation exhausts the tissues *in loco*. Probably, as we have seen (p. 230), recurrences of well-organized growths are often due to the influence of operative traumatism, and the same circumstance may contribute to a later genesis of cancer or sarcoma. In certain cases, the dispersion of a tumour by pressure or electrolysis would commend itself as a measure less likely to be in itself injurious. Since high organization is a mark of relatively high vitality and resistance in the surrounding tissues, it may be supposed that to this circumstance is due the occasional unassisted disappearance of benign tumours. Dr. Creighton, quoting Billroth to the effect that tumours of the breast occurring between puberty and the age of thirty tend to undergo spontaneous resolution, says, "It is also a familiar fact of surgical practice that the same class of tumours of the breast are sometimes dispersed by strapping, or by the application of cold, or by other means."*

Pressure produces this effect probably by its interference with nutrition. The cells perish from occlusion of vessels, and the remains are absorbed by the vessels of the living parts. The clinical history of cases of uterine myoma shows that a reduction of the nutritive supply to both the uterine tissues and their neoplastic offspring may be followed by disappearance of the latter. At the menopause when the functional activity of the uterus has ceased it is common for uterine myoma to cease to grow and sometimes they will cease to exist. Referring to this absorption of myomata, Mr. Lawson Tait says, "Such a phenomenon has been described by several authors; but it is just the sort of occurrence which it is difficult to believe in till it has been seen, and as I have seen it several times I believe in its occurrence."† A useful application of this fact may perhaps be made in treating uterine myoma and other tumours at an early period of life. No organs of the body are more readily influenced by abundance or deficiency of nutriment than the sexual organs, and pro-

* See a remarkable case reported by Walshe. Op. cit. p. 213.

† *Birmingham Medical Review*, January, 1889, p. 21.

bably both uterine myoma and mammary adenoma would be beneficially affected by a reduced dietary. Already it has become a recognized surgical procedure to remove the uterine appendages with a view to inducing an artificial menopause and the cure of myomata.

Passing now to tumours that are not well-organized, the first principle of treatment will be the recognition and removal of the causes. Indeed this must be the first principle in the treatment of all tumours but *a fortiori* in cancer and sarcoma. At the liminal stage of cancer of the lip, or tongue, or cervix uteri, and especially at the precancerous stage, the immediate and complete removal of causes may sometimes be hoped to suffice for a return to health. There is trustworthy evidence that so simple a measure may have this result in innocent tumours. Dr. Hunter Mackenzie* has called attention to the fact that "the operation of tracheotomy for certain varieties of laryngeal growths in children may be followed by the spontaneous disappearance of the neoplasms and accompanying thickening of structures, and complete return of the vocal cords to health."

CASE 141.—"A boy, aged about five years, was brought on account of difficulty of breathing. This trouble dated from an attack of laryngitis during measles a few months previously. The obstruction was situated in the larynx, but its exact nature could not be determined with accuracy on account of the restlessness of the patient. Tracheotomy was necessary, and was performed by me on April 19th. The child recovered rapidly from the operation, and continued to wear the tube for about a year, during which time there was laryngoscopic evidence of the presence of inflammatory thickening and warty-looking growths about the glottis. Towards the latter part of this time these gradually disappeared, the vocal cords cleared up entirely, and the tube was permanently withdrawn."

But early or late in malignant disease the removal of causes is imperative. After the arguments of the preceding chapters

* *Lancet*, vol. 1, 1889.

argument is not needed now to show that if the smoker whose tongue has become cancerous persists in smoking, the disease will persist. Owing to the very nature of the affection, as we apprehend it, no imaginable therapeutic measure is likely to be of the least avail while the causes continue. Therefore, before any attempt is made to rid the patient of a malignant tumour, attention must be given to the life-conditions of the part affected. In the tongue local irritation should be removed; in the breast effort should be mainly directed to establishing a lower degree of functional activity in the gland; and in cancer of the uterus abstinence from sexual intercourse should be enjoined.

This being the primary consideration in the treatment of malignant neoplasms, our next consideration will be the choice of means for removing the growth. We may call to our aid the forces with which the organism, as a whole, antagonizes the hostile advances of a tumour; the growth may be cut out with a knife or other instrument; it may be destroyed by means of the cautery or caustics; attempts may be made to disperse the mass by electrolysis or by the internal exhibition of chemical substances. Of each of these means it may first be said that the identity of the tumour units and the units of the tissues as respects their organic nature forbids the faintest hope of cure by internal medicines did not centuries of experience prove the measure futile. And when we bear in mind the qualities which give character to malignant tumours, we are discouraged from expecting to cure by electrolysis. Seeing how the elements of embryonic tumours tend to infiltrate the tissues both locally and systemically, their destruction in this way must be judged to be impossible. And with electrolysis, as with the treatment by caustics and the cautery, there is the likelihood of stimulating the tumour to more active growth. Escharotics are still resorted to by many, but I think quite sufficient reasons have been met with in the foregoing pages for looking with disfavour upon their employment. It should indeed become an acknowledged precept, in the

treatment of this class of tumour, to scrupulously avoid the introduction of any condition likely to promote the growth-activity. Among such conditions may be numbered exploratory punctures, the application of liniments, friction, the use of caustics and the cautery. Under special circumstances, perhaps, escharotics and electrolysis may be used with benefit. In attempting to cure malignant disease, or to minimize the evil effects of it, we take side with the organism against its enemy, and wherever war can be made upon the neoplasm, without at the same time making war upon the tissues, the patient will derive temporary or permanent advantage.

And what are the implications as regards the treatment of malignant neoplasms by excision? We have seen that if our conception of neoplasia is correct, and if we correctly interpret the clinical phenomena, operative traumatism tends to give a fillip to the disease. In advanced cases it probably does so to a marked degree. Is excision then to be condemned? By no means. There are facts and inferences to show that at an early stage, in accessible situations, and where the disease has not extended beyond narrow limits, extirpation by the knife may be permanently curative. This has been proved in cases of cancer of the lip and scrotum. There is ground, therefore, for hope that in other situations ablation at an early stage may result in a cure, and especially if attention be given to the removal of causes. But where the disease is far advanced, and the age and other conditions are favourable for its further extension, treatment by excision or any other means at present understood is without promise. Yet short of cure, in severe cases of malignant disease, particularly where the secretions of the tumour are poisoning the system, extirpation will, as surgical experience attests, prolong life and relieve suffering.

In § 44, on the prevention of tumour-disease, it was observed that undue systemic nutrition must probably be included among the conditions to be recognised and avoided. As to the influence of superabundant nourishment in promoting

the *growth* of tumours, the evidence is conclusive, and the application of this fact will often be of very great importance in the treatment of tumour-disease.

One other means of treatment is the assistance we may afford the organism in its efforts to resist and overcome a neoplasm. If the general health and strength be improved, the inroads of the tumour are rendered more difficult. Cases have been recorded, as the cases of atrophic cancer,* which show that a tumour may be held in check for long periods by what we must regard as the physiological resistance of the organism.

It is to be expected that future experience, guided by the higher conceptions we have purposed to develop, may yet lead us to therapeutic measures superior to any at present within the reach of deduction.

* See Bryant: Diseases of the Breast, p. 142.

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